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TROPICAL DISEASES BULLETIN

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BUREAU.

General Editor:
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COMMONWEALTH MYCOLOGICAL INSTITUTE
26 MAY 1971

London:
TROPICAL DISEASES BUREAU,
Imperial Institute, S.W.

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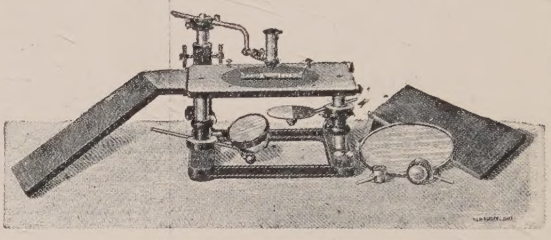

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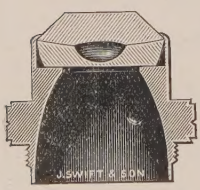

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TROPICAL DISEASES BUREAU.

TROPICAL DISEASES BULLETIN.

Vol. 2.] 1913. [No. 3.

KALA AZAR.

Experimental.

Basile (Carlo). **La Trasmissione sperimentale delle Leishmaniosi del Mediterraneo ai topi per mezzo delle pulci.** [The Transmission of Mediterranean Leishmaniasis to Rats by means of Fleas.] — *Atti della Reale Accad. d. Lincei. Rendiconti.* 1913. Apr. 6.

The author reminds his readers that he has shown that kala azar in the Mediterranean districts is transmitted amongst dogs and human beings by the human and dog fleas, and that in these the leishmania appear as flagellates which are morphologically distinct from the flagellates peculiar to these fleas. He has obtained a further confirmation of this view in the following manner.

On 25th and 26th January 1913, there were caught from a dog heavily infected with leishmania 200 fleas. These were fixed on wires by Nöller's method and kept at a temperature of 22° C. The day following their capture the fleas were made to feed upon a new-born dog in order that their faeces might be examined. Only three of the fleas showed flagellates of the type leishmania in their faeces. One was only slightly infected, the other two heavily. The two heavily infected fleas were dissected and an emulsion made in saline at 22° C. Part of this emulsion was injected intraperitoneally into two white rats, while the rest was made into films which showed abundance of flagellates. The marrow of the two rats was examined on February 26 by amputation of one hind limb and again on March 10 by removal of the other. Both these examinations were negative. On March 22 (56th day after injection) one rat was killed and in the hypertrophied spleen leishmania were discovered. This proves to the author that his views are correct and that the flagellates in the fleas were in reality leishmania.

[The reviewer has had some experience of Nöller's method (this *Bulletin*, Vol. 1, p. 367) and has found that the fixing and

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examination of a single flea may occupy an hour or more. Basile appears to have fixed, fed, and collected the excreta of 200 fleas in two days.]

C. M. Wenyon.

Scordo. **A proposito di Alcuni Tentativi d'Infezione delle "Anopheles" con Succo Splenico di Malati di Leishmaniosi Interna.** [Some attempts to infect Anopheles with splenic juice from Leishmaniasis patients.]—*Malaria e Malat. d. Paesi Caldi.* 1913. Mar. Vol. 4. No. 2. pp. 84-89. With 1 plate.

In a former paper (this *Bulletin*, Vol. 1, p. 633), the author described his attempts to infect Anopheline mosquitoes by feeding them on cultures of leishmania. He has now made similar experiments with the leishmania obtained directly from the spleen of a case of infantile kala azar. The blood which was rich in leishmania was treated in three ways. Firstly, some of it was placed on the surface of a disc of flesh over which was inverted a glass containing mosquitoes. Secondly, a piece of flesh was made to soak up some of the blood after which it was suspended in gauze in a glass with mosquitoes. Thirdly, some of the blood was injected into the superficial layers of the skin of a rabbit. The mosquitoes were allowed to remain for a quarter of an hour over the pieces of flesh when they were placed to feed upon the rabbit at the area of injection of the leishmania. About sixty mosquitoes were employed in the experiment and of these forty were eventually dissected after an interval of 24-48 hours or longer. In some of the mosquitoes no evidence was obtained of their having fed as there was no blood in their intestines. In others unaltered red blood corpuscles were present but never any leishmania. The salivary glands also gave negative results. As a result of these experiments therefore the author not only failed to obtain any evidence of a development of the leishmania in the mosquitoes but was unable to prove that the leishmania had been ingested.

In two smears made from the mosquitoes the author encountered an organism which he thinks is of protozoal nature and which is readily mistaken for leishmania on account of its similarity in size. The organism is pear-shaped with one extremity rounded and the other pointed, and is frequently grouped in clusters of six to eight enclosed in a kind of capsule which takes a pink tint in the stained films. Free forms are also present. There is a red staining nucleus at the centre and usually a more deeply staining granule at the pointed extremity. The author does not commit himself as to whether these correspond to the two nuclei of a leishmania. Division forms were not numerous though some with two nuclei were seen. The parasites were very numerous, as many as a hundred occurring in a single field of the microscope. The mosquito in which this organism was found was at the third day of experiment but there was no evidence, in the shape of altered or unaltered red blood corpuscles, that it had taken up any blood. This fact together with the numbers present has convinced the author that the organism is not a developmental

form of the leishmania. A coloured plate with thirteen figures illustrates this parasite, no previous reference to which can be found by the author.

C. M. W.

Scordo (Francesco). **Die Leukocyten des Meerschweinchens und des Kaninchens in Kontakt mit den Flagellatenformen der *Leishmania donovani* in vitro und im Körper der Tiere.**—*Centralbl. f. Bakt.* 1. Abt., Orig. 1913. May 3. Vol. 69. No. 1-2. pp. 85-89. With 1 plate.

This is a German translation of the author's paper which has already been reviewed (see this *Bulletin*, Vol. 1, p. 364).

C. M. W.

Epidemiological and Clinical.

Caronia (G.). **Weiterer Beitrag zur Leishmania Anamie.** [Further Contribution to the Study of Leishmaniasis.] — *Arch. f. Kinderheilkunde.* 1913. Feb. 20. Vol. 59. No. 5-6. pp. 321-347.

This paper contains an account of 37 cases of infantile kala azar which have been seen in the clinic for children's diseases at Palermo University since April 1911. Twenty pages are devoted to details of the history of the cases while the rest of the paper deals with general matters arising therefrom. As in former accounts of cases from Palermo it is again shown that the disease attacks especially the children of the labouring classes who live in small rooms together with all kinds of domestic animals. Infantile kala azar most usually commences in winter or early spring.

As regards the condition of the blood it was noted that in about one half of the cases there was a leucopenia while in the other half the number of white blood corpuscles was hardly changed from the normal.

There were only two cases of recovery out of the total of 37. Fifteen of the casese were examined with the object of testing the blood for the presence or absence of antibodies. In only one of these was there a partial fixation of the complement while in another case in which a recovery took place there was complete fixation. This case has been the subject of a paper by Di Cristina and Caronia (see this *Bulletin*, Vol. 1, p. 7). A study of the cases shows that they arise in several small centres scattered round Palermo. Only two cases arose in Palermo itself. The relation of dogs to the disease in children has been the subject of a special enquiry but only in one case was an infected dog found, in a centre to the north of Palermo; later in conjunction with Basile the author discovered another in Carini, an endemic centre 25 kilometres from Palermo.

As a result of his observations the author believes that the disease is not always acquired in the same way and that there exists in all probability a variety of mechanisms by which kala azar is transmitted.

C. M. W.

Spagnolio (G.). **Nota Clinica su Alcuni recenti Casi di Leishmaniosi Interna (Kala-Azar).** [Some Recent Cases of Kala Azar.]—*Malaria e Malat. dei Paesi Caldi.* 1913. Mar. Vol. 4. No. 2. pp. 80-82.—*Riforma Medica.* 1913. May 17. Vol. 29. No. 20. pp. 536-538.

In a paper published in November 1912 the author drew attention to fifteen cases of kala azar (see this *Bulletin,* Vol. 1, p. 361). He now gives a description of a further eleven cases from the district of Bordonaro in Sicily, one of which is apparently recovering. All the cases, which are typical, are in young children the eldest of whom is three and a half years of age. In only two had the children associated with dogs in their homes and in one the author knew the dog was perfectly healthy. He calls attention to the following three facts in connection with this series.—

1. In the houses from which the cases came lived other children of various ages who were in the best of health.

2. In two cases where children had previously died of the disease in the same house a considerable interval had elapsed between the death of one and the falling ill of the other.

3. No evidence could be obtained associating the occurrence of the disease in the children with the death of any dog in the vicinity of the house.

The author believes that these three factors render the canine origin of the human cases very doubtful and more so the idea that fleas are responsible for the transmission of the malady.

C. M. W.

Salvatore (Domenico). **Un Caso di Kala Azar a Derna.**—*Malaria e Malat. d. Paesi Caldi.* 1913. Mar. Vol. 4. No. 2. pp. 73-76.

The case described is that of a soldier who contracted the disease either at Derna or some other Italian town. The usual features were presented by the case which terminated fatally owing to violent haematemesis. Leishmania were discovered post mortem, thus confirming the diagnosis made clinically before death. The author points out that this, being a case in an adult, still further supports the view of Gabbi that no real difference exists between the Indian and Mediterranean diseases, for both of which there is the single parasite *Leishmania donovani.*

C. M. W.

Ciminata (Antonino). **Sul Reperto Parassitario nelle Anemie da Leishmania.** [The Finding of Parasites in Leishmaniasis.]—*Rivista Ospedaliera.* 1913. Feb. 28. Vol. 3. No. 4. pp. 156-159.

The author describes two cases of infantile kala azar which were examined post mortem. Smears made from the spleen and bone marrow and stained by Romanowsky stains did not reveal any leishmania though in an examination of sections of the various organs leishmania were seen in fair numbers in the

endothelial cells of the capillaries. Reference is made to a similar case seen by Di Cristina; leishmania were discovered in numbers in material drawn from the spleen during life though smears made from the spleen soon after death failed to show any; in sections however typical cells containing parasites were seen. This possible absence of leishmania in smears renders the diagnosis of kala azar very difficult. According to Di Cristina the disappearance of the parasites from the spleen soon after death, though they may have been present in large numbers before, is due to the presence in the blood of some lytic substance which destroys the majority of the leishmania.

[A similar case of the disappearance of leishmania soon after death was recorded by Lignos (see this *Bulletin*, Vol. 1, p. 4), and the case described by Archibald (see below) in which parasites could not be discovered in smears is of interest in this connection].

C. M. W.

Goretti (Girolamo). **Su di una Forma rara di Splenomegalia. Contributo Anatomo-Patologico.** [A rare Form of Splenomegaly.] —*Malaria e Malat. d. Paesi Caldi.* 1913. Mar. Vol. 4. No. 2. pp. 117-122.

The case described is that of a youth aged seventeen from Monteleone in Calabria, who suffered from fever with enlargement of the spleen. The disease terminated fatally and the author made a detailed examination of the organs, an account (five pages) of which is given. Though a careful search was made no leishmania could be discovered in any of the organs.

C. M. W.

Archibald (R. G.). **An interesting Case of Kala Azar.**—*Jl. R. Army Med. Corps.* 1913. May. Vol. 20. No. 5. pp. 512-521. With 1 plate.

The case is that of a young Arab, aged twenty, who fell ill in Khartoum with a disease which ultimately turned out to be kala azar contracted at Singa on the Blue Nile. A most interesting feature of the case was the failure to find leishmania in smears though puncture of the liver was performed four times and of the spleen three times. A diagnosis of kala azar was only obtained by the finding of leishmania in the liver of a monkey (*Cercopithecus sebaeus*) which had been inoculated intraperitoneally twelve weeks before, with material obtained from the case by liver puncture. Culture tubes of N.N.N. medium inoculated from the liver and spleen puncture material and incubated at 24° C. also failed to develop flagellates.

It was noted on the several occasions that liver and spleen puncture were performed that the material so obtained was of a granular nature, and in the stained smears peculiar "coccal bodies" were found of varying shades of blue and red and enclosed as a rule in cells. They resembled to all intents and

purposes large cocci more or less uniform in size massed together in the cells, which were devoid of nuclei and had a blue and often vacuolated protoplasm. In the cultures on N.N.N. medium, though no flagellates developed, the "coccal bodies" were present even after ten days though they showed no sign of development.

As regards the nature of the bodies the author is somewhat guarded in his views but he says they gave one the impression of being coccal organisms of a specially large type. He admits that the nuclei of some of the cells in the smears showed granular changes. Similar bodies had been previously found by the author in smears from another case of kala azar from the same district. He draws attention to the fact that CARTER and THOMPSON and BALFOUR record the presence of large coccal bodies in oriental sores of the non-ulcerating type, and SEIDELIN has recently described a coccus in four cases of dermal leishmaniasis from Yucatan.

As regards the examinations of the peripheral blood in this case, there was a great increase in the large lymphocytes, a change which in the author's experience is a very constant feature of kala azar in the Sudan. There was also an increase in the eosinophile cells which appeared to be unconnected in any way with skin lesions or worm infections of the gut. Leishmania were never seen in the blood films.

Though the case was undoubtedly one of kala azar as demonstrated by the monkey inoculation, the patient recovered without specific treatment.

C. M. W.

CRESPIN. **Leishmaniose et Paludism chronique infantile.**—*Caducée.* 1913. Apr. 5. Vol. 13. No. 7. p. 89.

The author gives a table illustrating the differences between the two easily confused diseases chronic infantile malaria and kala azar. In malaria there is the early and almost simultaneous appearance of the cardinal symptoms, fever, gastro-intestinal trouble, enlargement of the liver and spleen, oedema, and anaemia with an earthy colour of the skin. In kala azar the same symptoms appear, but slowly and successively—first the fever, then the intestinal symptoms, and finally the others.

In malaria the large liver and spleen are painful and tender and there are referred pains along the course of the phrenic nerve, while in kala azar these organs are neither painful nor tender and there are no referred pains. In malaria there is more usually constipation rather than diarrhoea while in kala azar the reverse is the case. In malaria oedema of the face and lower extremities is the rule, while in kala azar it is limited usually to the lower extremities. With malaria recovery is the rule after specific treatment, while in kala azar there is no specific treatment and the disease is incurable.

C. M. W.

Lombardo (Giacomo). **Contributo allo Studio delle Alterazioni Anatomiche dell' Anemia da Leishmania.** [Anatomical changes found in Leishmaniasis.]—*Pathologica.* 1913. May 15. Vol. 5. No. 109. pp. 292-296.

This paper contains a detailed account of the post mortem findings in a case of infantile kala azar from Catania.

C. M. W.

Treatment.

Caronia (G.). **Sulla Guaribilità dell' Anemia da Leishmania (a proposito di 8 casi di Guarigione osservati a Palermo).** [Eight Cases of Recovery from Leishmaniasis.]—*Malaria e Malat. d. Paesi Caldi.* 1913. Mar. Vol. 4. No. 2. pp. 90-96.

Though it was first held by Jemma that infantile kala azar always terminated fatally, Jemma, Basile, Nicolle and others gradually realised that a mild form of the disease existed and complete recovery was possible. Jemma described a case of recovery in a child five years old from Palermo and Nicolle another in a child of two from Tunis. Two other cases were recorded by Spagnolio in Messina and Lignos in Athens, while Jemma has had three further cases of recovery in Palermo. In the present paper the author gives an account of the cases of recovery met with at the clinic of Jemma at Palermo. Seventy-eight cases of infantile kala azar have been seen. Of these fifty have died, eight have recovered, while twelve are still living and eight have been lost sight of. Neglecting those living and those that have disappeared the percentage of recoveries is about fourteen. Outside Palermo other cases of recovery have been described by Nicolle, Spagnolio, Lignos, Petrone, and Caryophyllis and Sotiriades, making a total of fourteen recorded recoveries from infantile kala azar in the Mediterranean districts.

The author describes in detail the eight cases from Palermo. The ages varied from 21 months to five years and in seven cases leishmania had been discovered, usually in large numbers in smears from the spleen. In the single case in which leishmania had not been seen microscopically a dog inoculated with spleen pulp contracted the disease. As regards treatment various remedies have been used, but the author believes that in each case the cure resulted from natural processes though he is of opinion that arsenic, in whatever form administered, has a beneficial action.

C. M. W.

Roux (F.). **Arsenic in the Treatment of Kala Azar.**—*Indian Med. Gaz.* 1913. Apr. Vol. 48. No. 4. pp. 132-133.

The author has treated cases of kala azar by means of Ramalline, a French composition containing arsenic in the form of a compound of mineral and organic salts. This compound offers the great advantage over pure arsenic of being supported without ill result by the patient. It is administered

in the form of a pill containing 1 milligramme of arsenical salts and the patient is given eight pills a day. So far five cases have been treated with favourable results.

C. M. W.

Canine Kala Azar.

Basile (Carlo). **La Trasmissione sperimentale della Leishmaniosi naturale del cane ai topi conigli e cavia.** [The Transmission of Canine Leishmaniasis to Rats, Rabbits, and Guinea-pigs.] —*Atti della Reale Accad. dei Lincei. Rendiconti.* 1913. Mar. 16.

Two rats and two rabbits were injected intraperitoneally with an emulsion of the organs of a dog infected with leishmania. One rat was killed thirty days later and the slightly enlarged spleen was found to be infected with leishmania. The second rat is still under observation. The two rabbits killed on the thirtieth day gave a negative result, while similarly five young guinea-pigs were unsuccessfully inoculated intraperitoneally from the organs of an infected dog.

C. M. W.

Basile (Carlo). **Sulla Leishmaniosi nel cane e sull 'Esistenza di Leishmania nel midollo spinale di cani naturalmente infetti.** [Leishmaniasis in the Dog. Leishmania found in the Spinal Marrow of Naturally Infected Dogs.] — *Atti della Reale Accad. de Lincei. Rendiconti.* 1913. Apr. 20.

Canine kala azar is characterised clinically by fever, alopecia, wasting, and paraplegia of the hind limbs and can develop in either an acute or a chronic form. The acute type of disease attacks dogs of about five months of age, while the more chronic form is seen in older dogs, which frequently recover naturally and may be apparently healthy, though harbouring the parasite for considerable periods of time. In the chronic form, when a fatal termination is threatening, the nervous symptoms, involving especially the hind limbs, become more marked so that it would appear that there is some definite involvement of the nervous system. This view the author has confirmed by the finding of leishmania in smears of the spinal cord of two dogs naturally infected with kala azar. One of these dogs was presented to the author by the father of a child who was at the time suffering from kala azar. The dog was subjected to the operation of splenectomy for purposes of experiment but it died during the operation. The spleen was of normal dimensions, a fact which suggests to the author that forms of anaemia in children who have no enlargement of the spleen may still be kala azar.

La Cava was the first to demonstrate leishmania in the cerebro-spinal fluid of a case of human kala azar and the author now draws attention to this condition in dogs and points out that the nervous symptoms of both kala azar and trypanosomiasis are due to a similar cause.

C. M. W.

Tropical Sore.

Wenyon (C. M.). **A Further Note on a Case of Dermal Leishmaniasis from S. America, with the Results of Inoculation Experiments.**—*Jl. London School Trop. Med.* 1913. Apr. Vol. 2. Part 2. pp. 117-119.

This case has already been described (see this *Bulletin*, Vol. 1, p. 13). The present note deals with the subsequent history after treatment was commenced, the result of the culture of the leishmania obtained from it, and some inoculation experiments on animals.

It is recorded that the patient was treated in two ways, firstly by killed cultures of the leishmania injected subcutaneously and secondly by the application of an ointment made of equal parts of methylene-blue, lanoline and vaseline. This ointment was applied on a piece of lint the size of the sore both morning and evening. Healing quickly took place, apparently under the influence of the ointment.

Pure cultures were obtained from the sores and with these some inoculation experiments were carried out:—

"1. With the first culture obtained (Nicolle's culture virus) a human being was inoculated on the skin of the forearm in two places—one by intra-cutaneous injection with a hypodermic needle, and the other by scarification. A year has now elapsed since the inoculation and no infection has taken place.

"2. A young rabbit was inoculated intravenously on two occasions with rich cultures of the leishmania, but no infection took place.

"3. A young rabbit was inoculated intravenously on one occasion with rich culture, but did not become infected.

"4. Attempts were also made to infect mice by intraperitoneal injection of rich cultures, but without success."

With the virus obtained from the sore a dog and baboon were successfully inoculated but a small puppy injected intravenously failed to acquire the infection. Two mice inoculated intraperitoneally did not become infected. A cat inoculated in each ear developed small pinhead nodules after two months at the sites of inoculation. These have increased slightly in size and now, five months after inoculation, are still present, and leishmania have been discovered in them first by the culture method on N.N.N. medium and later by microscopic examination of smears from the sore.

Compared with a culture of *Leishmania tropica*, obtained from the oriental sore of Aleppo, the South American leishmania grew much more readily, though morphologically no constant differences could be made out between the two types of parasite.

G. C. Low.

Bates (L. B.). **Leishmaniasis (Oriental Sore) of the Nasal Mucosa.**—*Jl. Amer. Med. Assoc.* 1913. Mar. 22. Vol. 60. No. 12. p. 898.

The case here described is the fifth of oriental sore encountered in Ancon Hospital. The patient, a farmer aged 35,

had suffered from the disease for three years. There was ulceration of the helix of each ear, of the free margins of the alae nasi, and the extensor surface of each elbow, a partially healed ulcer over the sternum, and a nodule on the skin. Smears from the ears and alae nasi showed leishmania, as also did smears made from the nasal septum on each side. There was thus definite involvement of the mucous membrane of the nose by the leishmania. This is the first case with this complication noted from Panama and suggests that the dermal leishmaniasis of Central America is identical with the disease of South America where involvement of the mucosae has been frequently described.

C. M. W.

Escomel. **Première Découverte de *Leishmania tropica* flagellée dans le Corps Humain.** [Correspondence.]—*Bull. Soc. Path. Exot.* 1913. Apr. Vol. 6. No. 4. pp. 237-238.

The author writes that on September 6, 1911, he communicated to the *Sociedad medica d'Arequipa* his discovery of flagellated forms of leishmania in skin lesions. On two later occasions similar flagellates were discovered by him in other cases. He believes that this leishmaniasis is different from espundia and that the mucous membranes do not become involved. Accordingly he suggests that the organism should be distinguished under the name of *Leishmania americana* var. *flagellata*. A similar discovery of flagellated forms of leishmania was reported by La Cava (this *Bulletin*, Vol. 1, p. 370). Laveran, who presented this note to the *Société de Pathologie Exotique*, points out that it is premature to create a new species of leishmania on the occasional presence of flagellated forms in the lesions.

C. M. W.

Keelan (R. S.). **A Case of Bagdad Sores showing an apparently long Incubation period.** [Mirror.]—*Indian Med. Gaz.* 1913. Apr. Vol. 48. No. 4. p. 146.

The note refers to a native aged 55 who had been all his lifetime in Lucknow. He made one pilgrimage to Bagdad a year and a half after which there developed sores on his hand and legs. These increased in size and were identified as oriental sore by the finding of leishmania.

C. M. W.

SLEEPING SICKNESS.

Kleine (F. K.) & Eckard (B.). **Zur Epidemiologie der Schlafkrankheit.** [On the Epidemiology of Sleeping Sickness.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1913. May. Vol. 17. No. 10. pp. 325-328.

In those regions with which the authors are acquainted sleeping sickness exhibits a tendency to spread but slowly. An isolated focus of the disease was found in Maisome, an island in Lake Victoria. At the landing place there lived four infected persons who judging from their symptoms had been ill for two or three years. These people had never left the island and must have been infected in the place. Infected sailors of visiting boats had been the reservoir from which the fly had derived its infection. Although the island swarmed with *Glossina palpalis* the infection had not spread, and the remaining 500 inhabitants were healthy. A similar state of affairs was found in south Tanganyika by Stolowsky and also by Kinghorn and Montgomery (*Sleeping Sickness Bulletin*, Vol. 2, p. 384). The authors remark that the slowness with which the infection spreads in such regions is very astonishing. Horn (*Sleeping Sickness Bulletin*, Vol. 2, p. 224) and Kinghorn (*Sleeping Sickness Bulletin*, Vol. 2, p. 257) have explained the slow spread of the disease on the Gold Coast by the assumption that the population have acquired a certain degree of immunity. If, however, immunity occurred as a result of infection the number of healthy parasite carriers would be great, as is the case in malaria or in Texas fever or piroplasmosis of dogs. Experience in Uganda and German East Africa has shown, however, that the great proportion of the infected persons died in the course of a few years. A natural or an acquired immunity has not been observed.

Experiments were undertaken to ascertain whether the tsetse flies developed any immunity to the parasites. It was thought that possibly young tsetse hatched from the pupae of flies which had been fed on infected blood might have acquired a certain degree of immunity, which would inhibit the development of the trypanosomes in them when they were subsequently fed on infected blood. Since the antibodies formed by the mammalian host during trypanosome infection are not strongly specific, the possibility is not excluded that Glossina through taking up one species of trypanosome might become non-receptive for another. In order to obtain information on this subject a large number of female Glossina were fed alternatively on sleeping sickness monkeys and goats infected with *T. congolense*. By this means the formation of antibodies against trypanosomes should be stimulated in the body of the mother flies. After the course of three weeks the pupae were collected as they were deposited and the flies—434 in number—which were subsequently hatched, fed on sleeping sickness monkeys. On the eighteenth day the surviving 402 flies were killed and examined. Eleven, or 2·7 per cent., were found to be infected. In another series of 90 Glossina the experiment was continued for a month and then the flies were put to feed in batches on three different monkeys; all

three became infected, showing that of the 90 at least three were infective. This percentage corresponds to figures obtained under similar conditions with young Glossina whose ancestors had not been previously fed on infected animals in the manner described. There is hence no reason to believe that there are developed in the bodies of flies, by the daily taking up of trypanosomes, antibodies which are transmitted to the next generation.

The slow spread of sleeping sickness can therefore be no more explained by an immunity of Glossina than by an immunity of man. The critical point must be sought in the nature of the trypanosome itself. It is impossible to infect Glossina with certain strains. Moreover, it has been shown by various workers that climatic conditions exert an important influence on the development of the parasites in the tsetse flies.

[The work of Kinghorn and Yorke in the Luangwa Valley (*Sleeping Sickness Bulletin*, Vol. 4, p. 315) showed that the proportion of infective (with *T. rhodesiense*) to non-infective wild *Glossina morsitans* was about 1 to 500, and that whilst about 16 per cent. of the big game were infected with this parasite yet only a relatively very small number of cases of sleeping sickness exist. Thus in a district where there is a sufficient number of infective fly to infect 16 per cent. of the wild fauna the disease appears to be spreading but slowly amongst the human population. Such data as this seem to indicate that perhaps man is for some reason less easily infected than the lower animals. It must be remembered that amongst the wild fauna themselves there appears to be a great difference in susceptibility to infection; waterbuck, for example, were found by Kinghorn and Yorke to be frequently infected with *T. rhodesiense*, whilst zebra were never found to harbour the parasites.]

W. Yorke.

Schuberg (A.) & Böing (W.). **Ueber den Weg der Infektion bei Trypanosomen- und Spirochätenerkrankungen.** [The Track of Infection in Trypanosome and Spirochaete Diseases.]—*Deut. Med. Wochenschr.* 1913. May 8. Vol. 39. No. 19. p. 877-879.

Notwithstanding the enormous literature dealing with trypanomiasis little or nothing is to be found concerning the manner in which the parasites actually invade the vertebrate organism. Experiments were devised to obtain information on this subject.

In the earlier series a large number of punctures, of as little depth as possible, were made close together in a small area of skin. By this means the site of the punctures was easily found when sections of the skin were subsequently made. The punctures were made with the finest entomological needles. Infected blood was then dropped on the punctured area and allowed to remain there for some time. The behaviour of the ingoing trypanosomes was studied by examination of sections of the affected region. As by this method the number of invading trypanosomes was relatively very small the following technique was adopted in later experiments. Heavily infected blood, diluted with an equal volume

of 5 per cent. sodium citrate solution, was injected intracutaneously by means of a syringe. As far as possible the injections were made immediately under the epidermis or even into the corium, but not into the subcutaneous connective tissue. Owing to the thinness of the skin of rats and mice, which were the animals used, this procedure was quite easy. In the skin, and likewise in the subcutaneous tissue if this were pierced, distinct vesicles were formed which remained visible externally for several hours. This manner of introduction of the virus resembles closely that of the biting fly, with the advantage that many more parasites were injected and thus their behaviour could be more readily observed. In the earlier experiments the injected vesicles were situated on the abdomen, but later exclusively on the thigh because it was found desirable to examine the neighbouring lymphatic glands. Sections of the tissues involved were stained by Schuberg's modification of the Giemsa method. Experiments were carried out with *T. lewisi* and *T. brucei*.

By killing the various animals at different periods after the injection of infected blood and examining the tissues involved the authors were enabled to follow the path of the invading parasites.

The trypanosomes escape very quickly from the blood vesicle into the lymph spaces of the corium, and thence migrate through the subcutaneous connective tissue into the neighbouring lymphatic glands. In these sites they increase enormously in numbers and are to be observed in the glands of the same side of the body in large numbers before they can be found in the peripheral blood. It follows that the trypanosomes investigated (*T. lewisi* and *T. brucei*)—and probably all others—must be regarded not merely as blood parasites, but in not less degree as parasites of the lymphatic system.

The spirochaetes of relapsing fever and the fowl spirochaetes behave in a similar manner. They quickly escape from the injected blood and migrate into the surrounding connective tissue of the skin.

In a postscript Schuberg refers to the experiments of Uhlenhuth and Emmerich (this *Bulletin*, Vol. 1, p. 677) which demonstrated that *T. gambiense* and *T. equiperdum*, when injected directly into the testes of rabbits, multiply rapidly in these organs; and further that sometimes even when these parasites were injected intravenously, a greater increase of the trypanosomes was observable in the testes than in the blood stream and other organs. In view of the observations recorded in the present paper Uhlenhuth expressed the opinion that the explanation might be that the testes contain numerous lymphatics.

W. Y.

Heckenroth. **Tournée médicale effectuée sur le Congo et l'Oubangui.** — *Ann. d'Hyg. et Med. Coloniales.* 1913. Vol. 16. No. 1. pp. 104-144. With 3 maps.

The objects of this expedition, which started on September 25, 1911, were firstly to determine the therapeutic value of arsenophenylglycin in trypanosomiasis and secondly to obtain more precise information regarding the distribution of the disease.

The results obtained by treating sleeping sickness patients with arsenophenylglycin are published in another paper (this *Bulletin* Vol. 2. p. 35).

Distribution of human trypanosomiasis on the middle Congo and Oubangui.—The map published by the Commission to the French Congo in 1909, which is the only one we possess, required to be completed and revised. The number of natives examined was 9,359; direct examination of the blood and gland juice in conjunction with clinical examination was considered sufficient. The author studied successively the four districts of *Bangala, Bondjo, M'Baca* and *Banziri-Bouraca-Sangyo.*

Bangala extends along the French bank of the Congo from the northern extremity of the "Couloir" to the village of Liranga. Since 1907, when Leboeuf visited the country, the population has considerably diminished and in certain parts has completely disappeared. In four years the population of the village of Loukoléla has been reduced to one-half. The villages in the Bangala district can be divided into four groups, viz., Bonga, Loukoléla, Irébou and Liranga. The percentages of cases of sleeping sickness found at these were 3·87, 10·3, 5·69 and 9·93, respectively. It is interesting to note that in 1907 Leboeuf gave the following figures—Loukoléla 13·3 per cent., Irébou 16·04 per cent. and Liranga 15·5 per cent.

Bondjo extends on the Oubangui from the village of Boubangui to the great agglomeration of Ikoumba, a distance of about 350 kilometres. The results of examination of the population in the various groups of villages in this district are as follows:—Impfondo 5·24 per cent. infected, Doungou 1·3 per cent. (in one village, Boumba, 7 cases were found out of 39 persons examined), Bétou 7·9 per cent.

M'Baca.—The population of this district has been decimated by an exceedingly severe epidemic. It commences on the other side of Ikoumba and ends north of Bangui. Leboeuf visited one of the villages, Bimbo, of this district in 1907. He considered that the first case of the disease did not occur before 1906; nevertheless he wrote, "The disease is about to make real progress at Bimbo and before long a heavy mortality is to be expected." This prediction has soon proved true and the author found that 39 per cent. of the 403 persons examined were infected. The other groups of villages examined in this district were Mongoumba where 20·5 per cent. and Yacoli where 27·2 per cent. of the population were infected.

Banziri-Bouraca-Sango.—This district reaches on the banks of the Oubangui from Bangui to Mobaye. In the Mobaye group of villages 9 per cent. of the population were infected, in the villages between Mobaye and Konango 15·7 per cent., in the Konango group 14·4 per cent., in the Bessou group 8·5 per cent., in the Kémo group 12·5 per cent., and in those between Possel and Bangui 19·7 per cent.

The above figures only apply to villages which are on the banks of the Congo and Oubangui, but in addition persons coming from the interior were met and examined at several of the river villages. Time did not permit the author to visit many villages

lying some hours' march away from the river. Of 1,088 persons examined who came from such villages 5 per cent. were infected. There is little infection amongst the population who live constantly at a distance from the Oubangui. Those who, on the contrary, frequently visit the river as porters and labourers are fairly heavily infected. The author points out the necessity for supervision of the movements of natives, to protect regions still free from infection. The question is of the utmost gravity, since it is well known with what rapidity countries are devastated where trypanosomiasis assumes its epidemic form. Half of the population of the river has been annihilated in less than ten years.

Prophylaxis of human trypanosomiasis on the middle Congo and Oubangui.—Human trypanosomiasis has spread along the Congo and Oubangui to install itself at length on their tributaries, which with the commercial development and administrative occupation of the country have gradually become important highways; *e.g.* the M'poko, Lobaye, Tomi and Kotto.

As a rule the percentage of trypanosomiasis is greater in the factories and on the stations than in the neighbouring villages, but occasionally, especially during epidemics, it may be higher in the villages. This anomaly is perhaps only apparent, as during epidemics the natives who are in the employ of the European are better fed, lodged and clothed than their fellows in the villages. It is probably such factors that explain why Europeans are rarely infected although they may spend considerable periods in villages where 25-30 per cent. of the population are infected.

Glossina palpalis was found everywhere along the middle Congo and the Oubangui. Only two specimens of *Glossina fusca* were taken. It was found that the distribution of tsetse did not correspond with that of sleeping sickness, or more precisely, the "coefficient tsétsé" is far from explaining the mortality from sleeping sickness in all districts. For example at Bonga, Loukoléla and Irébou there are innumerable tsetse which are found even in the village clearings and make travelling by canoe a veritable torment. Notwithstanding this very high "coefficient tsétsé"—higher than in any other portion of the Congo or Oubangui visited by the author—very few cases of sleeping sickness were found. On the contrary in Mobaye and Kémo, where 15-30 per cent. of the population are infected, tsetse is rare on the French bank during this period of the year (December and January). The natives assert, however, that the fly is numerous on the Belgian bank. Under these circumstances the question arises whether any other biting fly is concerned in the spread of the disease. In the course of his tour the author carefully noted the biting flies found in each village and district visited by him. Mosquitoes, Stomoxys, Tabanidae, Simuliidae and the larvae of *Auchmeromyia luteola* were encountered in various villages. No definite relationship could be established, however, between any of these and trypanosomiasis. The question of the transmission of sleeping sickness in countries where the tsetse does not exist can be solved only by a prolonged series of transmission experiments.

In a table details are given of the number of cases found at the various villages in each of the four districts. In the Bangala country 1,012 persons were examined and 58 cases found, in Bonjo there were 170 cases out of 2,373, in M'Baca 569 out of 2,022 and in the Banziri-Bouraca-Sango group 437 out of 3,372. The total population was estimated at 19,000 and the number of cases of sleeping sickness 2,550. These figures show the necessity for measures which will tend to protect the country against the ravages of trypanosomiasis and to prevent its extension to new regions. In the bush only recommendations as to general hygiene, and simple measures of prophylaxis such as clearing, isolation of the sick, and notification of fresh cases are practicable. Isolation of infected cases is practised, but only concerns those in the last stages of the disease. Of the 1,250 cases recognised by the author only 20 were kept aloof by the inhabitants. Isolation indeed appeared to be to the native less a matter of safeguard than of personal embarrassment, resulting from a relative or friend becoming too troublesome. The unfortunate isolated ones, badly nourished and finally totally abandoned, quickly succumb. This is probably why so little sleeping sickness in the third stage is seen.

From the point of view of prophylaxis the length of time which the untreated survive is of importance. The author is able to give information touching certain cases noted by Leboeuf in 1907 which have remained untreated. At Loukoléla of 8 cases 2 have disappeared, 5 are dead and 1 is in good health on the Belgian side. At Irébou of 13 cases 4 have disappeared, 7 are dead and 2 are still living in the Belgian Congo. At Liranga of 14 cases 2 have disappeared, 1 died in 1907, 3 in 1908, 3 in 1909, and 2 in 1910. Of the remaining 3, 1 was in good health on the other bank and 2 were seen by Heckenroth and had apparently recovered.

W. Y.

Mitzmain (Maurice Bruin). **The Rôle of *Stomoxys calcitrans* in the Transmission of *Trypanosoma evansi*. — *Philippine Jl. Science.*** Sect. B. (*Philippine Jl. Trop. Med.*) 1912. Dec. Vol. 7. No. 6. pp. 475-518. With 5 plates.

This paper records a considerable number of precise experiments devised with the object of ascertaining whether *Stomoxys calcitrans* can transmit *T. evansi*. All attempts to demonstrate mechanical transmission were negative; nor was success met with in efforts to effect transmission by means of interrupted feeding. The only positive result obtained was in one of three experiments to ascertain whether mechanical transmission could be effected by successive interrupted feeds.

Further experiments were conducted to see if there was a cyclical development of *T. evansi* in the fly. Both wild and laboratory bred Stomoxys were used in these experiments. In the first experiment 14 wild flies were used. They were allowed to feed once on a heavily infected guineapig and subsequently were fed daily on healthy animals. The experiment was continued until the 18th day, when the sole remaining fly was too

enfeebled to feed. It was inoculated subcutaneously into a healthy guineapig. Neither this nor any of the healthy animals upon which the flies were fed became infected. Three other experiments in which 190, 60 and 90 laboratory bred Stomoxys were employed also gave negative results. In the first two of these the flies were fed on two consecutive days on infected animals and in the third on three consecutive days.

An account is given of some interesting observations on the relation of non-biting flies to Stomoxys in contaminative infections. An abnormal percentage of non-biting flies was generally found on collecting insects from domestic animals, and the majority of them were found on examination to be engorged with mammalian blood. A quiet bullock was selected for observation; some 150-200 flies, mostly muscids, were seen to collect on him. In a short time the author's attention was attracted to the peculiar grouping of the ecto-parasites; groups of 2 to 4 and 5 prevailed. On closer inspection the group was found invariably to consist of more than one species, a Stomoxys usually providing the central figure. Where this species was lacking it was found that the group fed from a common area with the heads of the individuals in close contact; the food was found to be a droplet of freshly exuding blood. It was noticed that even other blood-sucking flies found on cattle often take advantage of the action of the more powerful proboscis of the Stomoxys. *Lyperosia* was found to await its turn with the non-biting flies.

Experiments were conducted to determine the relationship of the common house fly, *Musca domestica,* to Stomoxys as a harbourer and carrier of trypanosomes. Numerous trypanosomes were found in the abdominal contents, 3 hours after the flies had been fed on the abraded tail of an infected monkey, and inoculations of the abdominal contents into guineapigs resulted in infection. In another experiment 30 laboratory bred Stomoxys were fed on a healthy monkey. Immediately they had fed 50 Musca which had fed on a fresh wound on a surra animal were substituted for the Stomoxys. Full opportunity was thus given them to carry infected material on labella and pulvillus into the wounds presented. The results of this and three similar experiments were negative.

Details are given of the technique employed in keeping Stomoxys for experimental work. The greatest difficulty was encountered in attempting to keep flies, in either small or great numbers, in a common enclosure.

Screened stable.—Here the difficulties presented are summed up in the presence of natural enemies. Particular reference is made to the common insectivorous lizard and the ubiquitous spider. Spraying with cresol was effective in dealing with these.

Glass vessels.—Large bottles and museum jars of three litres capacity were used. Thirty days was the longest time flies were kept alive in these containers. Untimely death resulted from mite infestation, cannibalism, and excess of moisture.

The use of individual glass tubes.—By this means the difficult problem of keeping the flies alive in captivity was most successfully solved. Ninety-four days was found to be the maximum

life of the adult Stomoxys, kept individually under laboratory conditions. A test tube of 24 mm. bore plugged with cotton was found the most convenient; moisture requirements were regulated by means of pieces of filter paper which were changed at least every two or three days. The tubes were not changed oftener than twice a week. The flies when not feeding were kept in the dark at 20-26° C.

The following summary is given—

1. Only negative results were obtained in the attempts at direct mechanical transmission of surra with flies which were induced to bite healthy animals at intervals ranging from five minutes to three days after being permitted to complete the feeding upon infected animals. Thousands of *Stomoxys calcitrans* were employed in 29 experiments involving the use of 3 horses, 6 monkeys, and 22 guineapigs.

2. Twenty-seven experiments were performed in attempts to transmit surra by the interrupted method of feeding. All attempts proved negative *where a single application of a varying number of flies was used*, as many as 38 on a horse, and a maximum of 40 on a small guineapig. The intervals between feeding on infected and healthy animals averaged twenty-five to forty seconds in the two instances cited.

3. In 3 trials, interrupted feeding was employed in successive daily applications. In attempting to determine the minimum number of bites necessary to infect an animal, as high as 40 were followed by negative results. The only positive result obtained was produced from a succession of 206 interrupted bites in which the flies were transferred immediately from the infected to the clean animal. The flies were applied thirty-two hours during a period of six days.

4. The results of these experiments indicate that *Trypanosoma evansi* does not develop in the body of *Stomoxys calcitrans*. Ninety-four days was the longest period in which laboratory-bred flies were tested for a cyclical development, and sixty-seven days the maximum for wild flies.

5. Organisms of surra were not found in *Stomoxys calcitrans* beyond eighteen hours after feeding on an infected animal, and the limit for infection by inoculation was ascertained in these experiments to be six hours.

6. Pathogenic trypanosomes were found in the proboscis of the fly thirty seconds after feeding on infected blood. Within one minute and thirty seconds the organisms were not present in the mouth parts in a form capable of infecting by inoculation into guineapigs.

7. The wounds made by the labium of *Stomoxys* were not found to be a suitable channel for infection. Consequently, it is not likely that surra in domestic animals is produced through this avenue by external contamination; namely, faeces, mouth parts, and pulvilli of infected flies.

8. The intimate relation in the feeding habits of *Stomoxys* and of house flies has been pointed out. *Stomoxys* has been demonstrated to provide through its bites the infection of *Musca domestica* and other dung flies. These flies have been demonstrated to act as carriers, harbouring the surra organisms for several hours.

9. No evidence was obtained to indicate that *Tr. evansi* is hereditarily transmitted to the offspring of *S. calcitrans*. The larva of this fly fed on surra blood does not continue to harbour the trypanosome and the fly is "clean" upon reaching maturity.

10. It is demonstrated that the individual glass-tube method is the most suitable for applying flies in feeding on experimental animals and for keeping flies for long periods under laboratory conditions.

The photographs illustrate the methods of keeping flies for transmission experiments.

W. Y.

Mitzmain (M. Bruin). **Collected Notes on the Insect Transmission of Surra in Carabaos.**—*Philippine Agricultural Review.* 1912. Dec. Vol. 5. No. 12. pp. 670-681.

The first portion of this paper deals with the dispersion of the lice of carabao—the Indian buffalo (*Bubalus bubalis*)—and their rôle in the transmission of *T. evansi.*

One thousand lice (*Haematopinus bituberculatus*), collected from a carabao whose blood contained numerous trypanosomes, were divided into five lots of 200 each. In one of these, set aside as a control, it was found that although the majority of the lice lived for two days none were alive after three days. The other four lots were fed on healthy carabaos 2, 10, 24 and 48 hours, respectively, after their removal from the infected host. Only that carabao became infected upon which the lice were fed which had been removed from the infected host but two hours previously.

It was found that the *Lyperosia* sp. fly which is common in the Philippines is responsible for the dispersal in nature of large numbers of the carabao lice. In a collection of 1,800 *Lyperosia* 620 lice were found attached to the flies: the lice were never found attached to Stomoxys or indeed to any other species than the Lyperosia.

It was observed that in carabao infected with surra the trypanosomes were frequently absent from the peripheral circulation for comparatively long periods. Susceptible animals were inoculated with the blood of infected carabao after these negative periods had lasted for from two to 26 days. As a result of these experiments it is concluded that during the negative stage of the disease the carabao is not a source of danger as an infective focus.

In an entomological study of a surra outbreak among carabaos *Lyperosia*, *Stomoxys*, *Tabanidae*, *Muscidae* (non-biting) were found in the various infected haciendas in the proportions given in the table.

Table II.—*Fly distribution.—Percentage according to host.*

——	Lyperosia.	Stomoxys.	Nonbiting Muscid.	Tabanids.
Cattle	70	10	20	3
Carabaos	95	3	2	specimens.
Horses	25	70	5	

The author points out that these observations are of but slight value as the study was of only two weeks' duration. He is of the opinion that the presence of carabao lice in unusual numbers, with due consideration to other insects, influences the incidence of surra.

An experiment was made to ascertain the relation of *Lyperosia* sp. to surra in carabaos. A fly-proof cage was so partitioned that two surra-infected carabaos and a healthy carabao could occupy adjoining stalls without bodily contact and still be

exposed to the bites of flies placed in the enclosure. In all, over 5,000 flies were employed in the experiment. The result was negative as the healthy animals did not become infected.

W. Y.

Treatment.

Kolle (W.), Hartoch (O.), Rothermundt (M.), & Schürmann (W.). **Ueber neue Prinzipien und neue Prepärate für die Therapie der Trypanosomeninfektionen.** [On New Principles and New Preparations for the Treatment of Trypanosome Infections.]—*Deut. Med. Wochenschr.* 1913. May 1. Vol. 39. No. 18. pp. 825-828.

This paper records the results of experiments to ascertain the value of various preparations of antimony as therapeutic agents in trypanosomiasis.

In the earlier experiments mice infected with nagana were employed. The strain killed the mice regularly within five days. An emulsion of metallic antimony in oil, injected intramuscularly, was found to produce acute toxic symptoms and death, in doses of 5 mgm. per 10 gm. of body weight of the animal. It was determined that 1 mgm. of metallic antimony was sufficient to cure the infection with certainty. The trypanosomes disappeared from the circulation within 24 hours and did not return. Unfortunately, metallic antimony even in this dose proved poisonous. All the animals treated with metallic antimony and also with most other active preparations of antimony used by the authors died from chronic poisoning. The mice, however, died sterile; parasites were not found in the blood nor in any of the organs and subinoculated animals did not become infected. Antimony trioxide was an exception as it proved to be much less poisonous. Many other metallic preparations were used, but except in the largest doses had no therapeutic action on trypanosome infections.

Experiments were undertaken to ascertain whether the therapeutic activity of the various antimony compounds had any relation to their chemical constitution. It was found that pentavalent compounds were not toxic except in large doses, but also that they were not active therapeutically. Trivalent preparations proved to be exceedingly toxic and at the same time of great therapeutic activity. It was established that for antimony compounds—soluble or insoluble, organic or inorganic—to be active, the antimony must be in the trivalent form.

"Trixidin" (30 per cent. emulsion of antimony trioxide in oil) was found to have an extraordinary valuable therapeutic effect. This compound only killed mice in doses of 100 mgm. per 10 gm. body weight, and is thus practically non-toxic. No symptoms of chronic poisoning were observed after its administration. Intramuscular injection of 1 mgm. per 10 gm. of body weight cured mice with certainty.

As a result of the first part of their investigations the authors state that with metallic antimony as with different insoluble organic and inorganic compounds of antimony, so long as these contain antimony in the trivalent form, they can with certainty

cure mice, infected with nagana, dourine or *T. gambiense,* by a single injection. The mice, however, died of chronic poisoning after the absorption of metallic antimony and many other preparations of antimony. Various trivalent preparations of antimony are, however, relatively but slightly poisonous. Trixidin is of all known antimony preparations the most active on intramuscular injection; this is manifested by its chemotherapeutic coefficient (1 : 100), the permanent sterilisation which it causes, and by the absence of acute or chronic toxic effects. Animals infected with trypanosomes can be permanently sterilised in 100 per cent. of cases by one or two intramuscular injections of absolutely non-toxic doses of Trixidin. The question of antimony intolerance thus loses its significance for the treatment of chronic trypanosomiasis in men and the larger animals.

A large number of preparations, the therapeutic action of which was investigated by the authors, are classified as 'inactive,' 'active but not of practical utility,' and 'active and of practical utility.'

The second portion of the work is concerned with finding some means by which the poisonous action of chemotherapeutically active insoluble preparations of antimony, which lead on intramuscular injection to chronic poisoning, may be averted. The authors made use of a principle which has proved to be of great value in the treatment of syphilis, namely, the inunction of compounds in ointment form. They succeeded in curing infected mice by systematic, frequently repeated inunctions of metallic antimony in the form of ointments. In a proportion of cases relapses occurred. Trixidin is not active when administered by this method. With organic, insoluble compounds (*e.g.*, Scheitlin's *Antimon-Antipyrin-Chlorverbindungen*) they succeeded in curing 60-70 per cent. of infected animals by this method. Acute and chronic poisonous symptoms do not follow inunction of insoluble antimony compounds which when injected intramuscularly or subcutaneously are toxic.

As a result of the second portion of their work the authors conclude that it is possible to cure a great proportion (66 per cent.) of the smaller animals (mice, rats, guineapigs, rabbits and monkeys) infected with dourine, nagana or *T. gambiense*, by inunction of metallic antimony or certain insoluble combinations, without the slightest toxic effect. In contradistinction to 'Therapia magna sterilisans' the authors designate this form of antimony treatment as 'Therapia mite curans.' The principle of the employment of insoluble organic preparations of antimony either in ointment form or through the formation of intramuscular depots may be suitable for the treatment of chronic trypanosomiasis in man or the larger animals.

The paper concludes with the statement that in Trixidin is found a remedy, which, in respect of its chemotherapeutic index and its permanent effect, far surpasses all others hitherto employed in the therapy of trypanosomiasis. The effect of the drug is to be tested in sleeping sickness patients and large animals infected with trypanosomiasis.

W. Y.

Immunization.

Darling (S. T.). **The Immunization of Large Animals to a Pathogenic Trypanosome (*Trypanosoma hippicum* (Darling)) by Means of an Avirulent Strain.**—*Jl. Exper. Med.* 1913. May 1. Vol. 17. No. 5. pp. 582-586.

The object of this paper is to show that immunization of large animals can be effected by means of an avirulent strain of a pathogenic trypanosome (*T. hippicum*), that immunized animals completely recover from the infection and that they cannot be reinfected by the same strain nor by a virulent strain of the same species.

In a previous paper (*Sleeping Sickness Bulletin*, Vol. 4, p. 193) the author drew attention to the possibility of reducing the virulence of a strain of *T. hippicum* by selection from a guineapig.

Two mules, a dog, and a guineapig were inoculated from an infected guineapig which survived for the exceptionally long period of 336 days. These animals all recovered. Details are given of the two experiments with mules. The first mule was inoculated from the guineapig on the 279th day of the disease, and at the same time two other mules were inoculated with a virulent strain to serve as controls. The incubation period in the controls was 8 days, whilst in the other animals it was 11 days. All three animals were treated with arsenic according to Holmes's method (*Sleeping Sickness Bulletin*, Vol. 2, p. 359). The controls died on the 44th and 105th day respectively. In spite of the arsenic medication trypanosomes remained in the first mule's blood for 6 months after the arsenic had been discontinued. The animal was definitely infected and passed through a typical attack of the disease, becoming very emaciated. Ultimately, it recovered and its condition improved until, 13 months after inoculation, auto-agglutination had disappeared and its blood inoculated into a white rat and a guineapig did not give rise to infection. The second mule was infected by means of *Musca domestica* (*Sleeping Sickness Bulletin*, Vol. 4, p. 182) with the same avirulent strain. The incubation period was prolonged to 10 days, showing that the strain was avirulent. [As the incubation period of the control animals was 8 days the increase in the mules infected with the avirulent strain was only 3 and 2 days respectively. Such a slight increase in the incubation period hardly appears sufficient to warrant this statement.] The disease ran much the same course as in the previous mule and the animal ultimately recovered. This animal was not treated medicinally.

One animal, specially tested, was observed to be immune to the same strain and resisted infection to a virulent strain as well.

The author concludes by stating that he believes that the production of subliminal infections by means of avirulent strains will yield efficient immunity against subsequent infection from a virulent strain, and the danger from a recrudescence of virulence within the immunized animal and the infection of other animals would appear to be nil.

W. Y.

T. RHODESIENSE & T. BRUCEI.

BEVAN (Ll.). **Report on** *Trypanosoma rhodesiense*. *MS.*—Report to the British South Africa Company. Dated March 20, 1913.

The author gives an account of the morphology of the parasite found in rabbits infected with a Zululand strain of *T. brucei*. The infected animals were sent to him from Pretoria. The parasite was polymorphic; typical long forms with free flagellum, intermediate forms, and short stumpy forms were seen. Among the latter were a few having the nucleus in the posterior third.

As the disease progressed, the posterior-nuclear forms increased in number and several were encountered with the nucleus actually posterior to the blepharoplast.

After calling attention to the fact that it was on this posterior displacement of the nucleus that STEPHENS and FANTHAM based their diagnosis of a new species of human trypanosome (*T. rhodesiense*), the author refers to the fact that YORKE and BLACKLOCK have observed similar forms in a strain of *T. equiperdum*, BLACKLOCK in a strain of *T. brucei* [Uganda], and WENYON in a strain of *T. pecaudi*. This feature then, in a strain of trypanosomes from the Luangwa Valley or Sebungwe District, can no longer be regarded as evidence of a new species.

[The Royal Society Commission has already described posterior nuclear forms in a strain of nagana obtained from Zululand (this *Bulletin*, Vol I., p. 671). They consider *T. rhodesiense* (Stephens and Fantham) to be identical with *T. brucei* (Plimmer and Bradford). This, however, is doubtful as it has been shewn by STEPHENS and BLACKLOCK that *T. brucei* (Plimmer and Bradford) is a monomorphic parasite and easily distinguishable from either *T. rhodesiense* or *T. brucei* of the Uganda ox, to which they have given the name *T. ugandae* (this *Bulletin*, Vol. I., p. 662). At the present time it would appear that if the name *T. rhodesiense* is to be dropped it must be in favour of *T. pecaudi*. As regards the presence of posterior nuclear forms in *T. rhodesiense*, Bevan seems to have revised his opinion, for in previous papers (*Sleeping Sickness Bulletin*, Vol. 3, p. 21 and Vol. 4, p. 214) he indicates that he had been unable to find these forms in this strain.]

W. Y.

LAVERAN (A.). **Au sujet du** *Trypanosoma rhodesiense* **et du** *Tr. brucei*.—*Bull. Soc. Path. Exot.* 1913. May. Vol. 6. No. 5. pp. 340-343.

The author quotes the statement of the Royal Society's Commission that "evidence is accumulating that *T. rhodesiense* and *T. brucei* (Plimmer and Bradford) are identical" (see this *Bulletin*, Vol. I., p. 661). These authors base this view chiefly on a study of the biometric curves of the two trypanosomes and on the fact that the nucleus is sometimes in the posterior position in *T. brucei* as in *T. rhodesiense*. LAVERAN holds that the conclusion of the Royal Society's Commission would be admissible only if they demonstrate (1) that the means of identification

employed by them are infallible to the extent that one can dispense with all others, (2) that the trypanosome named by them as *T. brucei* is in reality *T. brucei* (Plimmer and Bradford). Neither one nor the other of these postulates is above criticism. The author continues by discussing the value of biometric curves for the differentiation of trypanosomes. It is difficult to believe that the biometric method is infallible. Duke has arrived at the conclusion that one can only accord to such curves a limited importance (see this *Bulletin*, Vol. 1, p. 137). The work of Muriel Robertson on the cycle of *T. gambiense* in the vertebrate host (see this *Bulletin*, Vol. 1, p. 44) shows that curves of this trypanosome are likely to be dissimilar. Again it has been shown by Wenyon and by Laveran and Nattan-Larrier that posterior nuclear forms occur in *T. pecaudi* and by Yorke and Blacklock that they are also encountered in a strain of *T. equiperdum*. The posterior position of the nucleus in certain individuals of *T. brucei* does not then warrant its identification with *T. rhodesiense*.

It is questionable if the trypanosome of Uganda which was used in the researches of Bruce and his collaborators is identical with *T. brucei* (Plimmer and Bradford).

In his classification of the pathogenic trypanosomes (*Sleeping Sickness Bulletin*, Vol. 3, p. 356) the author has placed *T. brucei* among the monomorphic trypanosomes, whilst *T. rhodesiense* figures amongst the dimorphic.

Stephens and Blacklock have recently shown that *T. brucei* of Zululand (Plimmer and Bradford) is monomorphic, whilst that from Uganda is dimorphic. They conclude that the two are not identical and propose for the Uganda parasite the name *T. ugandae* (see this *Bulletin*, Vol. 1, p. 662). If the Uganda trypanosome proves to be identical with *T. rhodesiense* as Bruce and his colleagues consider, it is unnecessary to give it a new name, but Laveran believes that it will be necessary to prove the identity of the two and considers the method of cross immunization peculiarly applicable.

In conclusion reference is made to previous experiments of the author wherein he showed by cross immunization that *T. brucei* is different from *T. rhodesiense*. (*Sleeping Sickness Bulletin*, Vol. 4, p. 135.)

W. Y.

South American Trypanosomiasis.

Chagas (Carlos). **Thireoidite Parasitaria.** [Parasitic Thyroiditis.] —*Rev. Med. de S. Paulo.* 1912. Sept. 15. Vol. 15. No. 17. pp. 337-350. With 8 figs.

This paper was read before the Medical and Chirurgical Society of S. Paulo.

In his introductory remarks the author gives an account of the history of the disease, and of the experiments by which it was proved that *Schizotrypanum cruzi* is transmitted by the 'barbeiro,' as the insect is called in Minas Geraes. He points out that this bug has been wrongly included in the genus *Conorhinus*;

it really belongs to the genus *Triatoma*. The principal transmitter is *Triatoma megistus;* another is undoubtedly *Triatoma sordidus*. Recent investigations have shewn that *Triatoma geniculatum* transmits a parasite found in the armadillo which is supposed to be identical with *Schizotrypanum cruzi*.

The Triatoma, or 'barbeiro' as it is familiarly called, infests preferably those residences which are of primitive construction, and the walls of which have numerous chinks offering hiding places for the insect. Under favourable conditions they multiply prolifically, and are present in enormous numbers in houses which have been infested for some time. They transmit the disease during all three stages of their life cycle. The winged insect may live longer than a year. Its total life period including all stages is approximately two years. The insect lives in houses that are occupied. Empty houses are quickly abandoned by the Triatoma which migrate in search of food.

The parasite *Schizotrypanum cruzi* is found in the posterior intestine of the Triatoma either as Crithidial forms or as the adult trypanosomes; the presence of the latter is regarded as indicative of infectivity of the insect. There is some difficulty in demonstrating the presence of trypanosomes in the salivary glands, where they lie in the interstitial tissue between the glandular cells.

In the human organism *Schizotrypanum cruzi* is only found in the peripheral blood in any numbers during the acute stage of the disease. In chronic forms the parasite is found more abundantly in the tissues. Evolution of the parasite within the human body occurs in two ways, (1) the flagellate penetrates the tissues, especially the muscles, becomes rounded and undergoes successive binary division, (2) in the pulmonary tissue the parasite divides more regularly into eight equal units. The former of these is believed to be multiplication of the 'indifferent' forms, whilst the latter represents that of the 'sexual' forms. The young forms have at first only a nucleus and blepharoplast, later they become flagellated and get into the circulation. The forms from the lungs enter the erythrocytes and become intracellular parasites. The organs chiefly attacked by the parasites are the central nervous system, heart, suprarenals, testicles, uterus, ovaries, and striated muscle.

Clinical and epidemiological observations.—The disease is most frequent during the hot months (October to March), owing to the greater proliferation of the 'barbeiro' during this period. Only in children was the acute form observed: in adults the disease was chronic and was the result of infection acquired during childhood. The disease may be inherited—babies of from 15-20 days having been found to be infected. An autopsy performed on a foetus shewed macroscopic lesions typical of the infection.

The manifestations of the disease are multitudinous; clinically the cases can be divided into acute and chronic. The acute infection is characterised by high temperature and numerous trypanosomes in the peripheral blood, it is often complicated by intense meningo-encephalitis and in these cases death occurs in a few days. There is often a mucoid infiltration of the subcutaneous

tissue causing the facies typical of myxoedema. The thyroid gland is so constantly involved that the term parasitic thyroiditis has been used to describe the disease. The pulse rate is frequently diminished to 40 or in rare cases to 30 or even 20.

Parasitic foci and inflammatory processes of great intensity are seen in the central nervous system. Cerebral diplegia is common. As a rule, patients with diplegia are idiots. Infantilism is generally accompanied by complete idiocy, though cases were met with exhibiting only slight mental deficiency. Cases of infantilism are very common. [For further details Chagas's previous paper should be consulted (*Sleeping Sickness Bulletin*, Vol. 4, p. 341.)]

W. Y.

Tramonti (E.). **Alcune considerazioni sulla malattia di Carlo Chagas (Thyreoiditis parassitaria).** [Some Observations on Chagas's Disease (Parasitic Thyroiditis).] — *Policlinico.* Sez. prat. 1913. May 18. Vol. 20. No. 20. pp. 697-701.

This paper is a review of the clinical features of schizotrypanosis. There is constant evidence in this disease of glandular insufficiency, on the part of the thyroid gland and suprarenals.

The clinical classification must depend on the predominant symptom, as the forms which the disease assumes are very various and not always sharply defined. The author divides the cases into two clinical categories, acute and chronic. Cases in which there are no acute morbid phenomena clinically, but in which the parasite is found in the peripheral blood by simple examination of fresh films, are grouped under acute. The acute form is subdivided thus:—(1) Those cases in which the nervous system is involved, *meningo-encephalitic* form. In this form the death rate is high and in any case the prognosis is unfavourable, paralysis, idiocy, and imbecility resulting. (2) Those in which the nervous system is not involved. Here the prognosis is better, the patient passing into a chronic state without serious impairment of function.

The chronic form is divided into five clinical groups—(a) *pseudomyxoedematous*, (b) *myxoedematous*, (c) *cardiac*, (d) *nervous*, (e) *chronic forms with acute crises.*

Mention is made of the group, *metaschizotrypanosis*, formed by Chagas, for those cases of infantilism, old goitre, and other morbid conditions consecutive to the disease.

Many cases of paralysis, aphaeresis and idiocy in children or infantilism in adults presented at the same time other clinical signs of Chagas' disease, while all endeavours to discover some other etiological factor such as syphilis or toxic, infective, or hereditary conditions, proved negative. The author finds from the evidence at autopsy that Chagas is justified in creating a 'nervous' form of schizotrypanosis. Multiple foci scattered in different parts of the brain reveal their presence clearly by clinical signs, so much so that one might say that Chagas's disease provides an excellent means of cerebral localization.

The most common motor disturbance is diplegia of cerebral origin, in which spastic symptoms predominate over paralytic.

The fact that parasitic foci are present on both sides of the brain or spinal cord explains the bilateral character of the paralysis. Athetotic and choreiform movements are frequently marked, the upper limbs being most affected and chiefly the fingers. The degree of loss of intelligence does not correspond to the amount of motor disturbance. Cases of complete idiocy shew sometimes very slight motor affection.

Speech is profoundly altered, total aphasia being common. Many cases present the clinical feature of pseudobulbar paralysis. Oculomotor paralyses occur, single muscles or several being affected. In cases of severe lesion of the nervous system general convulsions occur.

The author refers in some detail to two nervous cases in which post mortem examinations were made, one a child of three years, the other an adult of twenty-four, a complete idiot. In each case numerous parasites were found in the striped muscles. The author asks if it may not be possible that the endemic cretinism of the Alpine Valleys presents analogies in its aetiological mechanism to parasitic thyroiditis.

W. Y.

Unclassed.

Laveran (A.) & Marullaz (M.). **Au sujet du *Trypanosoma talpae*.**—*Compt. Rend. Soc. Biol.* 1913. May 16. Vol. 74. No. 17. pp. 1007-1008. With 1 text-figure.

The authors briefly review the previous literature on *T. talpae*. They examined 12 moles captured around Tournan (Seine-et-Marne), of which eight showed a very few trypanosomes while in one the parasites were not so rare.

The trypanosomes move too quickly to examine in detail in fresh preparations. In stained preparations only adult flagellates were found, which were 25μ to 27μ in total length and 3·5μ to 4μ in total breadth. The free portion of the flagellum is 3·5μ to 4·5μ. The undulating membrane is relatively straight. The posterior part of the body, 6μ to 7μ long, is drawn out in a spur-like manner. The blepharoplast is on one edge of the body, while the oval nucleus is on the opposite border. Chromophile granules occur in the cytoplasm. A text-figure indicates these characteristics.

The authors were unable to cultivate the trypanosome on a simplified Novy medium, and their attempts at inoculating the organism into 2 mice, 1 guinea-pig and 1 white rat were negative.

H. B. Fantham.

Ogawa (M.). **Studien über die Trypanosomen des Frosches.** [Studies on the Trypanosomes of Frogs.]—*Arch. f. Protistenkunde.* 1913. Apr. 19. Vol. 29. No. 2. pp. 248-258. With 1 plate and 3 text-figures.

The paper contains the results of Ogawa's work on *Trypanosoma rotatorium* of frogs. The main results of this, together with those of Frl. Mendeleeff-Goldberg and Doflein, were set forth recently by the latter author (see this *Bulletin*, Vol. 2, p. 42).

Ogawa describes two main forms of the trypanosome: (1) "ribbed" (2) smooth, as observed both in the internal organs of the frog *Rana esculenta*, and in cultures. Full morphological details are given, cyclical variation in the condition of the nucleus being of the most interest. The formation of non-flagellate from flagellate forms by protoplasmic concentration, retraction of the undulating membrane and abandonment of the flagellum is described fully. Some stages of the parasite contain an enormous number of fat globules, their appearance suggesting that they are degeneration products. This is not the case as the fat is reserve food, and also these flagellates divide vigorously.

Large aggregation rosettes (100μ diameter), the result of the intertwining of the flagella of many organisms, occur on both old and new cultures.

In conclusion, the author points out the possibility of demonstrating trypanosomes by cultural methods when they cannot be detected in the blood.

H. B. F.

Ponselle (A.). **Technique pour la Coloration des Trypanosomes et Trypanoplasmes de Culture.**—*Compt. Rend. Soc. Biol.* 1913. May 23. Vol. 74. No. 18. pp. 1072-1073.

The technique, specially suitable for flagellates in culture, is as follows:

1. *Fixation.*—Pour on the dried smear a quantity of the following mixture, sufficient to cover it:—

Absolute alcohol, 50 cc.

Tincture of Iodine (of the French Pharmacopoeia), 10 drops.

Allow this to act for 5 minutes. Wash in absolute alcohol and leave to dry.

II. Then pour on the preparation some drops of serum, sufficient to cover it completely. Horse-serum, heated to 56°, serves very well. Leave for 5 minutes. Wash in distilled water.

III. Stain for 15 to 30 minutes with Giemsa solution diluted in the usual manner (1 drop to 1 cc. of neutral distilled water). Wash in distilled water. Dry.

H. B. F.

RELAPSING FEVER.

Nicolle (Charles), Blaizot (L.), & Conseil (E.). **Etiologie de la Fièvre Récurrente. Son Mode de Transmission par les Poux.** —*Ann. Institut Pasteur.* 1913. Mar. 25. Vol. 27. No. 3. pp. 204-225.

During an epidemic of relapsing fever which raged in Tunis from February to August 1912, the authors were able to make a number of observations on this disease, which is usually very rare in Tunis. In this region relapsing fever has been known for a long time under the name of typhus, and both seem to be confounded in the native name "m'ard qmel," signifying louse disease.

Additional evidence in support of the view that relapsing fever is transmitted by the louse is afforded by the history of an outbreak during the last epidemic. A workman from Tripoli carried the infection to a "fondouk" in Tunis, of which two rooms were occupied by a colony of his compatriots. Shortly afterwards everyone of these persons became infected. As the result of a minute examination of the contents of the rooms, two fleas and one bug were found, and mosquitoes and Stomoxys were entirely absent. On the other hand, body and head-lice were present in enormous numbers.

The experiments recorded in the present article have been previously published elsewhere (see this *Bulletin*, Vol. 1, pp. 32-34).

E. Hindle.

Kleine (F. K.) & Eckard (B.). **Über die Lokalisation der Spirochäten in der Ruckfallfieberzecke (*Ornithodorus moubata*).** [On the Localisation of Spirochaetes in the Relapsing fever Tick.]—*Zeitschr. f. Hyg. u. Infektionskr.* 1913. May 20. Vol. 74. No. 2. pp. 389-394.

The authors have examined the organs of forty-five females of *Ornithodorus moubata* obtained from a native hut on the shore of Lake Tanganyika. The ticks had not fed for two to three weeks. By microscopical examination of organ films twenty-three of these ticks were found to contain spirochaetes, the parasites occurring most frequently in the ovaries, and in descending order in the coxal glands, Malpighian tubules, cephalic glands, stomach, and salivary glands.

A number of ticks were fed singly on separate monkeys and afterwards examined for spirochaetes. Whenever a monkey became infected as a result of the bite, spirochaetes were found in the organs of the tick. The converse, however, was not true, for ticks were frequently found to contain spirochaetes without producing infection by their bite.

In another experiment monkeys were injected with the ovaries of single ticks, some of which had been used in the preceding series.

Combining the results of the two experiments it appears that out of eighteen ticks in which spirochaetes could be detected microscopically, thirteen were able to produce infection in monkeys, whilst out of nineteen ticks that were free from spirochaetes not one produced any infection. Therefore the presence of spirochaetes, as such, seems to be necessary in order to produce infection. The authors add that the parasites multiply by transverse division sometimes producing short forms. The presence of comma shaped bodies was frequently observed but in no case was any infection produced by injecting them into monkeys, and therefore they are not considered to represent any stage in the life-cycle of the spirochaete.

In addition the authors found spirochaetes present in a large proportion of the eggs laid by infected ticks.

E. H.

Wittrock (O.). **Beitrag zur Biologie der Spirochaeta des Rückfallfiebers.** [The Biology of the Spirochaetes of Relapsing Fever.]—*Zeitschr. f. Hyg. u. Infektionskr.* 1913. Apr. 25. Vol. 74. No. 1. pp. 55-60.

The author fed a number of "clean" first-stage nymphs of *Ornithodorus moubata* on monkeys infected with *Spirochaeta duttoni*. At intervals of one hour and 1, 2, 3, 4, 6, 10, 14, 18, 22, 24, 73, 75, and 96 days respectively, the contents of one or more of these ticks were inoculated into healthy monkeys which all became infected. The results show that there is no non-infective period of development corresponding with that of trypanosomes in the intermediate host, and the author considers that this furnishes additional support for the view that there is no relation between spirochaetes and trypanosomes.

In conclusion the author criticises the view that the "chromatin granules" in ticks represent any stage in the development of the spirochaete, for he has found these granules in the unfed offspring of uninfected *Ornithodorus*.

E. H.

The Occurrence of Relapsing Fever in Somaliland. — Received in Colonial Office May 12, 1913.

Dr. R. E. Drake-Brockman, Medical Officer at Bulhar, records the outbreak of an epidemic of relapsing fever in Bulhar. In the "haffa" of Midzan, no less than fifty per cent. of the inhabitants were infected with the disease. Fortunately the mortality is said to be very low, but the incapacitating power of the disease is considerable owing to the number of relapses.

Large numbers of *Ornithodorus savignyi* were found in and around the infected "haffas," but no examples of *O. moubata*, and therefore the observer is of the opinion that the relapsing fever of this district is transmitted by the former species of tick.

[The occurrence of relapsing fever in Somaliland has been previously recorded by Brumpt, who also showed that the infection could be transmitted by *Ornithodorus savignyi* as well as *O. moubata.*]

E. H.

Lafforgue. **La Courbe Thermique dans la Fièvre Récurrente.**—*Bulls. et Mems. de la Soc. Med. des Hôpit. de Paris.* 1913. Mar. 13. 3 ser. Vol. 29. No. 9. pp. 579-581.

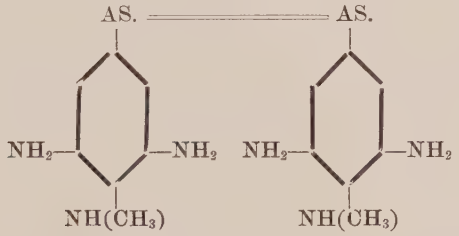
Amongst 22 cases of relapsing fever observed by the author in Tunis, eight showed very atypical temperature charts somewhat recalling "intermittent malaria." The patients presenting these atypical symptoms were all in a very bad state of health from other causes and it is suggested that this may have been the reason of the irregular character of the fever. Lafforgue points cut that it is only possible to be certain of the diagnosis of relapsing fever by examination of the blood, for the temperature is liable to be uncertain.

In conclusion the author states that he and Comte attempted to verify Tiktin's suggestion that relapsing fever is transmitted by bugs, but their results have been constantly negative.

E. H.

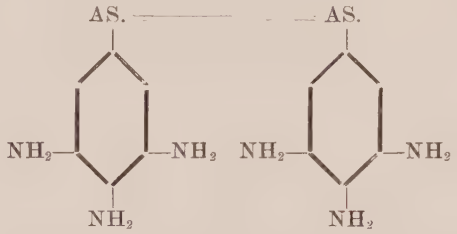
Giemsa (G.). **Beitrag zur Chemotherapie der Spirochätosen.** [Contribution to the Chemotherapy of Spirochaetoses.]—*München. Med. Wochenschr.* 1913. May 27. Vol. 60, No. 21. pp. 1074-1078.

This article contains an account of the therapeutic action on certain spirochaetal infections of a new compound, *dimethyldiaminotetraminoarsenobenzol*, prepared by Ach and Rothmann in the laboratory of C. F. Böhringer & Söhne and patented by this firm. This compound has the following constitution:—



and seems to combine a low toxicity with a very considerable therapeutic action. The author has tested its effect on infections of *S. gallinarum* in both fowls and canaries, *S. recurrentis* in mice, and syphilis in rabbits. The relation $\frac{\textit{dosis curativa}}{\textit{dosis tolerata}}$ was found to be 1/32 for *S. gallinarum* in fowls, 1/87·5 for the same infection in canaries, 1/1·56 for *S. recurrentis* in mice, and 1/12·7 for syphilis in rabbits. These relations compare favourably with those of salvarsan (fowl spirochaetoses 1/58, *recurrentis* 1/2·7, rabbit syphilis, 1/7 to 1/10).

In conclusion the author discusses the relation between chemical constitution and therapeutic action. The introduction of methyl (CH_3) groups into compounds has been found to lower the trypanocidal action, and therefore one would expect that hexaminoarsenobenzol—



—would be still more parasiticidal than the dimethyl derivative described above. Apparently this is the case, for the minimum effective dose of the latter compound is 0·011 gms. per kilo for rabbit syphilis, and 0·0014 gms. per 20 gm. mouse for *recurrentis*, whilst the corresponding effective doses of hexaminoarsenobenzolchlorhydrate are only 0·008 gm. and 0·00033 gm. respectively. No further information is given regarding this substance but the author states that he is continuing investigations on the subject. Other amino derivatives of arsenobenzol are in course of preparation and there seems every hope of still more effective compounds being obtained.

E. H.

Bronfenbrenner (J.) & Noguchi (H.). **On the Resistance of Various Spirochaetes in Cultures to the Action of Chemical and Physical Agents.**—*Jl. of Pharmacology and Experimental Therapeutics.* 1913. Mar. Vol. 4. No. 4. pp. 333-339.

The authors have investigated the resistance of various spirochaetes and also *Bacillus coli* to the action of different chemical compounds and temperatures. The spirochaetes were all grown on solid media and before being exposed to the various substances were mixed with 0·9 per cent. saline. The following spirochaetes were employed:—*Treponema pallida* (heavy type), *T. pallida* (small type), *S. refringens*, *S. mucosum*, and *S. microdentium;* and the action of the following substances is recorded: $HgCl_2$, As_2O_3, trikresol, phenol, saponin, sodium taurocholate, NaOH, HCl, gentian violet, alcohol, salvarsan and neosalvarsan. Especial attention was paid to the effect of the last two substances because of their therapeutic importance.

The results are given in tabular form from which it appears that in these experiments the toxic effects exerted by the chemicals on spirochaetes are from twenty to one hundred times greater than on *B. coli*. The sterilizing property of salvarsan is practically the same as that of neosalvarsan; the toxic effects of the latter substance are increased from two to five times and possibly more in the presence of enzymes from the liver, and especially those from the blood.

Spirochaetes suspended in physiological salt solution are killed at a temperature of 45° C. in from seven to ten minutes.

E. H.

Nicolle (Charles) & Blaizot (L.). **Deuxième Note sur la Courte Durée de l'Immunite dans le Fièvre Récurrente expérimentale.**—*Bull. Soc. Path. Exot.* 1913. Apr. Vol. 6. No. 4. pp. 242-243.

The authors continue the history of a monkey that, after an interval of less than six months from its recovery from an attack of spirochaetosis, had been reinfected a second time by an inoculation of the same virus (see this *Bulletin*, Vol. 1, p. 621). Seventy-four days after recovery from this second attack, this monkey was again inoculated with the same virus and suffered from a third attack of spirochaetosis, showing that no marked immunity had been developed as a result of the two previous infections. This observation confirms the authors' view that the crossed immunity reaction is not a safe method of distinguishing the various races of the *recurrentis* group of spirochaetes.

E. H.

Hidaka (S.). **Zur Frage der Beziehungen zwischen Syphilis und Recurrens-Immunität.** [The Question of the Relations between the Immunity against Syphilis and that against Relapsing Fever.]—*Zeitschr. f. Immunitätsforsch. u. experiment. Therapie.* 1913. Apr. 14. Vol. 17. No. 4. pp. 443-448.

The author has injected monkeys, infected with syphilis, with *Spirochaeta duttoni*, and also injected monkeys that had recovered from an attack of the latter infection, with syphilis, in order to determine whether the immunity was specific in each case. The results show that recovery from an attack of *S. duttoni* infection confers no immunity against syphilis, and conversely, animals infected with syphilis (in the so-called "Anergic" state of infection) are not immune against infection with *S. duttoni*.

E. H.

Nakano (H.). **Uber Immunisierungsversuche mit Spirochaeten-Reinkulturen.** [Studies on Immunity employing Cultures of Spirochaetes.]—*Arch. f. Dermatol u. Syphilis.* Orig. 1913. Mar. Vol. 116. No. 1. pp. 265-280.

Employing cultures of *Spirochaeta* (=*Treponema*) *pallida* the author has investigated certain immunity reactions of this organism, and his results are of interest for comparison with those obtained with the blood spirochaetes.

When spirochaetes from cultures, killed by heating to 60° C., were injected into rabbits, the serum of the latter was found to develop agglutinins and was active in dilutions of one in sixty to one in seventy, though not beyond. Precipitins could not be found.

With regard to the fixation of the complement, it was found very difficult with the various unspecific antigens that could be employed to decide whether the reaction was specific. Nevertheless there was a suggestion of the existence of such a reaction.

In the serum of the above mentioned rabbits, substances which dissolved spirochaetes were present in small quantity. In vitro, and in the sera of syphilitic human beings, such substances could not be detected.

An attempt to actively immunize rabbits by the injection of cultures of spirochaetes gave negative results and similar results were obtained on employing a vaccine prepared from human patients. The serum of these rabbits had a protective but not a curative action on rabbit syphilis.

Spirochaetes in the living body have a strong resistance against energetic cytolytic substances. Even after the injection of ten per cent. antiformin solution into a primary lesion in quantities sufficient to produce necrosis, living spirochaetes were still present.

E. H.

Launoy (L.) & Lévy-Bruhl (M.). **Les Variations Numériques et Morphologiques des Globules Blancs chez les Poules infectées de** *Spirochaeta gallinarum.*—*Compt. Rend. Soc. Biol.* 1913. Apr. 18. Vol. 74. No. 13. pp. 754-756.

Fowls infected with *Spirochaeta gallinarum* were found to present fairly regularly two waves of hyperleucocytosis. The first is often very little marked and is coincident with the infection, whilst the second does not appear until the spirochaetes are disappearing from the blood. The two are separated by an interval of comparative leucopenia. The variations in the leucocytic formula are fairly constant; there being an excess of polynuclears during the infection, and an excess of mononuclears after the crisis. The polynuclears belong to two types: at first there is an excess of pseudo-eosinophiles "a bâtonnets," and later of neopolynuclears with spherical granulations.

Although these variations are present, they are not specific, since they may be found in fowls suffering from tuberculosis and also certain intoxications.

E. H.

Gleitsmann. **Ueber die Beziehungen der Borrelien (Spirochäten) zu den Wirtszellen.** [On the Relation of Borreliae (Spirochaetes) to the Cells of the Host.] — *Centralbl. f. Bakt.* 1. Abt., Orig. 1913. Apr. 16. Vol. 68. No. 5-6. pp. 493-497. With 1 plate.

The first part of this paper is devoted to a criticism of Leonid Fränkel's view (see this *Bulletin*, Vol. 1, p. 42) that spirochaetes are parasitic on the leucocytes. By means of the dark ground illumination the author has carefully examined the blood of fowls infected with *S. gallinarum* and mice infected with *S. recurrentis* and finds no evidence to support the view that the spirochaetes ever actively penetrate into the white cells. Occasionally they may be seen within the red corpuscles, but in every case the latter seem to be injured and Gleitsmann is of the opinion that the spirochaetes do not penetrate uninjured cells.

By means of Buchanan's modification of the Levaditi-Yamamoto method, the author claims to have observed terminal flagella in *S. novyi*. The blood was not previously centrifuged, so therefore the appearances cannot be explained as the result of this process, as was the case in Zettnow's preparations.

With regard to the nature of the swellings often seen along the length of the spirochaete and the mode of division the author does not come to any definite conclusions, but figures are given suggesting the occurrence of longitudinal division.

[The reviewer had previously expressed the opinion that Leonid Fränkel's theory was based on a study of artefacts (*loc. cit.*) and Gleitsmann's observations confirm this view. The so-called terminal flagella figured by the author seem to be merely the drawn out extremities of the pellicle of the spirochaete.]

E. H.

Gross (J.). **Sporenbildung bei Cristispira.** — *Arch. f. Protistenkunde.* 1913. Apr. 19. Vol. 29. No. 2. pp. 277-292. With 1 plate.

The author describes the process of spore formation in *Cristispira tapetos*, a spirochaete which occurs in the crystalline style of *Tapes decussatus*.

The parasite merely breaks up into a number of short segments in a manner closely resembling the formation of coccoid bodies, or chromatic granules, in *Spirochaeta duttoni* and *S. gallinarum*. The latter part of the paper is devoted to a consideration of the nomenclature of the spirochaetes occurring in molluscs.

E. H.

MALARIA.

Bates (John Pelham). **A Review of a Clinical Study of Malaria Fever in Panama.**—*Jl. Trop. Med. & Hyg.* 1913. May 15. Vol. 16. No. 10. pp. 145-153. With 3 charts.

The author points out that the teachings regarding the course and treatment of malaria by the best authors in text books as recent as 1905 are variable and somewhat confusing. During his stay in the Panama Canal Zone from 1904 until the present time over eight thousand cases of malaria (including all varieties) have passed under his notice. He found that under thorough quinine treatment the fever invariably subsided in one, two, or four days. Occasionally it did not subside till the fifth or very rarely till the sixth day. Consequently in 1907 he stated as an axiom that any fever that did not yield to quinine in five days was not malaria, or at any rate if a fever should continue for more than five days, with quinine properly administered, there was something other than malaria which was causing its continuance. Rogers laid down a very similar axiom in 1908, and Deaderick in 1909 also stated that four days was the maximum period of resistance to quinine. Craig in 1909 stated that the symptoms are easily controlled within a week although in rare instances the plasmodium may be very resistant to quinine and persist for eight to ten days. He advocates a dose of about two grammes (thirty grs.) daily. Castellani and Chalmers in 1910 however, while agreeing that four days of quinine treatment reduces the temperature and symptoms in cases of quartan and benign tertian, state that this is not always the case with regard to the subtertian (malignant tertian) fevers. They assert that they have met with cases in which the fever has remained unaffected while the parasites can be found in the peripheral blood, notwithstanding several weeks' quinine therapy by various methods. The author points out however that these authors are not quite definite as regards the amount of quinine which they administered in their resistant cases. In consequence he still holds to his axiom and thinks that there is insufficient evidence to support the belief that certain strains of malarial parasites are resistant to quinine. The continuance of fever in cases of malaria after four or five days of thorough quinine treatment (at least thirty grains daily) is due in his opinion to some underlying obscure disease such as kala azar, typhoid fever, or uncinarial anaemia. The latter is very liable to be confused with malaria on account of the irregular fever. Hirsch pointed out that uncinarial anaemia was always looked upon as malarial cachexia until about 1885. Kala azar also was formerly considered as a kind of malarial cachexia. Three charts are given of cases of typhoid fever; in one of these malarial parasites were found. These disappeared under quinine treatment but the fever continued; a blood culture however gave a growth of *B. typhosus* and showed the true nature of the disease.

[This is a very excellent paper with a full list of references. Those interested should consult the original.]

D. Thomson

James (W. M.). **The Canal Zone Treatment of Malaria.** [Correspondence.] — *Southern Med. Jl.* 1913. May. Vol. 6. No. 5. pp. 347-349.

The author states that in giving quinine in the treatment of malaria, there are two factors to be considered (1) The solubility and absorbability of the drug; (2) The amount of the drug that is taken up by the patient.

It is much better to give quinine in liquid form as it is then more readily absorbed than when in the form of pills and powders. This is important since the gastro-intestinal tract is often congested and irritated in acute malaria, so that its powers of absorption may be greatly diminished. Sometimes cases of malaria which are resistant to quinine given by the mouth may be rapidly cured by hypodermic administration of the same drug. He has found that malaria is often more difficult to cure by quinine treatment when it is complicated by certain conditions such as, anaemia, acute gastro-intestinal congestion, stasis, constipation, organic disease, tuberculosis, and especially syphilis. He states that the cause of relapses in malaria is not yet known with certainty, but the majority favour the view that they are due to the resistant forms of the asexual parasite. It is best therefore to treat a malarial attack vigorously with quinine, as small and insufficient doses do not completely kill all the parasites, but tend to favour the development of these resistant forms. This is why relapses so often occur after insufficient treatment with quinine in small or irregular doses. After eight years of experience in treating thousands of cases of malaria in Panama, the following is the routine method adopted: —

(1) Give a preliminary purge, three to five grains of calomel. This is followed in twelve hours by two ounces of a fifty per cent. solution of magnesium sulphate.

(2) An initial dose of twenty grains of a liquid preparation of quinine sulphate is given. (This preparation is made by dissolving five grains of quinine sulphate in one dram of distilled water with a drop of concentrated hydrochloric acid.)

(3) Fifteen grain doses of quinine (same preparation) three times daily are then given for a week, or for five or six days after the temperature is normal. The dose is then reduced to thirty grains daily and continued for ten more days. In Panama this treatment has proved much more satisfactory in preventing relapses than the former treatment of ten grains three times a day. If the infection is very severe the dose is increased to fifteen grains four times a day.

(4) When vomiting is present, quinine is given in doses of twenty-two and a half grains (1·5 grams) hypodermically. A French preparation of the bi-hydrochloride is used (obtained in ampoules). Each dose is given well diluted in twenty cc. of normal salt solution, and injected deep into the subcutaneous tissues with a large syringe. Abscesses are very rare after this treatment.

(5) The above treatment does not always prevent relapses, especially where there have been previous relapses due to insuffi-

cient treatment at the commencement. In such obstinate cases the author injects intravenously by means of a "606" apparatus, doses of one to two grams of quinine in 300-500 cc. of normal saline, on two succeeding days and then continues with forty-five grains a day by mouth as noted above.

(6) Tonics with arsenic, iron and strychnine are valuable adjuvants in treating the anaemia resulting from malaria. But small doses of quinine added to these have no curative value, but rather tend to increase the resistance of any remaining parasites,

D. T.

Kirk (William Redin). **The Early Recognition of Tuberculosis with Especial Reference to its Confusion with Malaria.** — *Southern Med. Jl.* 1913. May. Vol. 6. No. 5. pp. 300-303.

The author points out that early cases of tuberculosis which present few physical signs may be easily be mistaken for malaria in a malarious country, since in early cases of tuberculosis one finds occasional rises of temperature with sweating and anaemia. This mistake of course would not occur if the blood were examined carefully for the plasmodia, before quinine is administered. In order to avoid it he advises careful examinations of the blood at intervals. The temperature should be taken frequently. It is important to get a careful history of the case, and if possible one should employ the different tuberculin tests, examine the sputum, and make a very careful physical examination.

D. T.

Van Poole (G. M.). **A Case of Quinine Idiosyncrasy.**—*Military Surgeon.* 1913. Feb. Vol. 32. No. 2. p. 192.

The author describes a case of remarkable idiosyncrasy to quinine in a soldier. At 5.15 p.m. three-fifths of a gramme (rather less than ten grains) of quinine in tablet form was administered by mouth for prophylactic purposes. At 6.15 p.m. a telephone message was received stating that the patient was dying. He was hurriedly brought into hospital where it was found that he was in a comatose condition, from which he could not be aroused. His face was cyanosed. The radial pulse was very rapid and almost imperceptible. The pupils were widely dilated and acted very sluggishly. The breathing was shallow and stertorous, and the skin cold and clammy.

His stomach was washed out, heart stimulants were given hypodermically and heat was applied externally. At 7.15 p.m. he was still cyanosed but he could be roused by shaking. Pulse 118, pupils dilated but reacted readily, breathing slow and deep, temperature subnormal. He made an uneventful recovery.

Most authorities agree that in cases of pronounced cinchonism the heart's action becomes feeble and slow. In this case the pulse was rapid, but might have become slow later on, had he not been treated so promptly.

D. T

Mühlens. **Bericht über eine Malariaexpedition nach Jerusalem.** [Report of a Malaria Expedition to Jerusalem.]—*Centralbl. f. Bakt.* 1. Abt., Orig. 1913. May 3. Vol. 69. No. 1-2. pp. 41-85. With 6 plates and 5 text-figs.

Malarial investigation.—The total number of blood examinations was 7,921 from over 7,000 different people, *i.e.*, about one-tenth of the population of Jerusalem.

Of the 7,921 blood samples 2,071 contained malarial parasites, *i.e.*, 26·1 per cent. were infected.

The degree of infection varies greatly in the different districts of the town according to the class of population. In the inner Arab quarters, in the unhygienic districts, the infection amounts to 25-40 per cent. of all inhabitants; in the Jewish quarters within the city walls the infection is at least as high, if not higher. Similar percentages are obtained in the Jewish colonies outside the city walls. In the European settlements outside the city walls (not counting the native servants) 10-25 per cent. were infected; in Bethlehem 10-20 per cent. School children were found infected up to 37·4 per cent.

The species of parasite most frequently met with was the malignant tertian. Benign tertian was next in frequency, and quartan was less common. (In Bethlehem three quarters of all cases were tertian.)

Table I. illustrates the degree of infection among the different groups of the population.

Table II. and Fig. 3 illustrate the monthly distribution of the different species of parasites. The principal malarial season is from July to October.

During the five months of this expedition six cases of blackwater fever occurred, four of which were seen by Mühlens himself.

Anopheles were found everywhere and in places were very numerous; they all belonged to the species *A. bifurcatus*.

Fig. 4 gives a record of the rainfall in Jerusalem. The propagation of the mosquitoes is in close relationship with the cistern method of water supply. The total number of cisterns in Jerusalem might be estimated at from 5,000 to 6,000 or even more.

Preventive measures.—No systematic anti-malarial measures had been taken previous to the author's arrival. General sanitary measures would in his opinion be also very good anti-malarial measures. The abolition of all cisterns, or even a general and efficient screening of the cisterns is regarded as impracticable on account of the enormous cost, not mentioning other great difficulties. Good results were partially obtained with quininization. Instruction in the schools, &c., is strongly advocated. The paper is well illustrated.

D. T.

Sehrwald (Ernst). **Zur Geschichte der Malariaübertragung.** [Contribution to the history of the transmission of Malaria.] —*München. Med. Wochenschr.* 1913. May 13. Vol. 60. No. 19. p. 1040.

This is a brief account of Stanley's efforts to prevent attacks of fever whilst in Africa. The author relates how Stanley received the statement of Emin Pasha that he had succeeded in preventing attacks of fever by the use of a mosquito net.

D. T.

Prophylaxis.

Hermant. **Fonctionnement du Service de Vente de la Quinine d'Etat dans la province de Nghê-An en 1912.**—*Bull. Soc. Med. Chir. de l'Indochine.* 1913. Apr. Vol. 4. No. 4. pp. 231-233.

In French Indo-China the state quinine is put up in tubes of ten tabloids, each containing 0·25 grammes of the sulphate. The price is 192 francs per 1,000 tubes. During 1912, 10,245 tubes, equal to 25 kilogrammes of quinine, were sold in the various depots. Beneficial results followed the distribution of the quinine, but the author gives no details or statistics.

D. T.

Giemsa (G.). **Das Mückensprayverfahren im Dienste der Bekämpfung der Malaria und anderer durch Stechmücken übertragbarer Krankheiten.** [The Mosquito-spray Method in the Campaign against Malaria and other Mosquito-borne Diseases.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1913. Mar. Vol. 17. No. 6. pp. 181-190.

The author describes certain improvements in the construction of the apparatus designed by him for the spraying of culicicide fluids. The composition of the fluid which he now advocates for use with his apparatus is as follows:—Pyrethrum tincture (20 parts of powdered pyrethrum blossom in 100 parts of 96 per cent. methylated spirit), 580 grams. Potash-soap (as free from odour as possible), 180 grams. Glycerin, 240 grams. For use dilute with twenty times its weight of water.

The fluid, which has been brought on the market in Germany as "Mückenfluid," causes hardly any damage to furniture or inconvenience to the operator. The cost of spraying a room of about 3,000 cubic feet is calculated to be approximately sixpence. Three figures illustrate different models of the apparatus.

D. T.

Graham (J. D.). **Further Experiments in School Quininisation in the Districts of Meerut and Aligarh, 1911.**—pp. 22 + 7. With 2 maps and 30 tables. Report published by Local Government, United Provinces, India.

The author maintains that the quininisation of the school children in Meerut and Aligarh (India) during 1911 has produced results as successful as those in Muttra in 1909 and in

Budaun in 1910. He claims that this method of combating malaria is suitable for general adoption, but that the help of the district staff is required and also an attitude of sympathy on the part of the schoolmasters. The measure has been popular in all localities.

His statistics show that it causes a reduction of the splenic index as well as a reduction in the malaria rate. Large doses of quinine apparently produce a more rapid diminution in size of the spleen than smaller doses. He concludes that eighteen grains of quinine (sulphate tabloids) should be the minimum weekly dosage for the adult male community. Children are given doses in proportion to their age. The method of giving quinine twice weekly on 'alternate' days is apparently the most efficacious. A careful register should be kept wherever prophylaxis is being attempted.

D. T.

Jackson (Thomas W.). **The Malarial Problem with Special Reference to Education and Diagnosis.**—*Interstate Med. Jl.* 1912. Nov. Vol. 19. No. 11. pp. 929-933.

The author points out that the statistical information regarding the true prevalence of malaria in the United States is not very reliable or accurate. The first reason of this is that in the average community deaths from malaria are not proved by microscopic blood examination, and again many latent cases which are perfectly capable of propagating the infection are missed. The only way to rectify this state of affairs is to educate further the physician as well as the laity, since the latter are still sceptical that malaria is propagated by the mosquito. He urges also the importance of making accurate sanitary surveys for malaria, as well as a blood census of the inhabitants and especially the children in malarious districts. Having obtained the desired data, efforts to cure the infected populace and to suppress the malaria-carrying mosquitoes should naturally follow. With regard to the infrequency of microscopic diagnosis of malaria in the United States, he makes the following statement:—

"During the year 1909, in a large laboratory connected with a metropolitan hospital, where more than twenty thousand new patients from all corners of the globe were treated and where a special feature is made of the teaching of malaria, only fifty eight of twelve thousand laboratory examinations made were blood examinations for malaria. This is something of an index of the failure of physicians generally to make use of the most direct and infallible diagnostic procedure in medicine."

D. T.

Monkey Malaria.

Blanchard (R.) & Langeron (M.). **Le Paludisme des Macaques. (*Plasmodium cynomolgi*, Mayer, 1907).**—*Arch. de Parasit.* 1913. Mar. Vol. 15. No. 4. pp. 529-542. With 2 plates.

The authors state that it is very rare to find plasmodial parasites in monkeys bought in Europe. In 1911 however they bought a monkey (*Macacus cynomolgus*) which happened to harbour plasmodia in its blood. The infection in this monkey was mild.

Two other monkeys were inoculated subcutaneously with its blood, with the result that one of them died in twelve days from a very acute infection. The other showed only a mild and somewhat latent infection and lived a long time. In the first inoculated monkey the plasmodium appeared on the seventh day after inoculation, on the eighth day there were chiefly ring forms, on the ninth day they had become rosette bodies. On the tenth day the monkey was very ill and it was observed that the rosettes had broken up again into young ring parasites, very similar to the young rings of *Plasmodium falciparum* in man. They measured 3μ to 5μ in diameter. The containing red corpuscles develop granules resembling those of Schüffner in the case of benign tertian malaria. On the eleventh day the blood of the monkey showed marked anaemia and the parasites were found to have grown so large as almost completely to fill the containing red corpuscle. On the twelfth day the animal was dying, so it was killed in order to get the organs and blood in a fresh condition.

No young rings were found in the blood but various other stages of the parasites, from young compact globules to rosette forms. Some showed commencing segmentation with two, four and six chromatin masses while the rosettes showed eight, ten or thirteen merozoites. Pigment appeared in the small globular forms as a single grain, and became more plentiful as the parasites increased in size. Numerous pigmented leucocytes were found. The organs showed a much greater abundance of parasites than the blood, and it appeared that the capillaries were obstructed by considerable numbers of rosette forms. The spleen contained enormous numbers of parasites and great abundance of pigment, contained especially within the mononuclear cells. The endothelial cells of the liver also were loaded with pigment. The appearance corresponded exactly to that found in human malaria. This disease resembles therefore in almost all its aspects an attack of pernicious malaria in man. The authors consider that the parasite is identical with those which have been described by Mayer, Flu, Mathis and Léger.

The corpuscles which contain the parasites remain normal in size, but invariably develop Schüffner's granules. The number of merozoites in the rosettes varies from eight to thirteen. This agrees with the finding in Mayer's parasite, but the parasite of Mathis and Léger appeared to form, almost always, sixteen merozoites.

The authors also observed the presence of gametes. The macrogametes were large globular parasites, filling the corpuscle almost completely. The protoplasm had an intense blue colour, the nucleus was generally excentric and stained a deep red colour. They contained abundant pigment, very black and in large grains. The microgametes were also large and globular, the cytoplasm stained a feeble rose or violet colour, while the nucleus which is large stains a pale rose colour. Mayer has observed that the gametes appear in the blood two days after the verification of the presence of parasites from an inoculation. The duration of the cycle of schizogony in this parasite is forty-eight hours.

In their conclusions, the authors state that this parasite observed by them in the *Macacus cynomolgus* is identical with the *Plasmodium cynomolgi*, Mayer, 1907. It is a distinct species, differing from the *Plasmodium inui* of Halberstädter and Prowazek, 1907, in the presence of Schüffner's granules and the form of the pigment. *Plasmodium cynomolgi* may be very pathogenic to the *Macacus cynomolgus* when it is inoculated into an animal which has not been immunised by a former attack. This pathogenic action takes the form of pernicious attacks of fever, accompanied by a heavy parasitic infection of the whole circulation. The pathological lesions produced are similar to those observed in man in pernicious malaria.

The article is illustrated by two coloured plates.

D. T.

Blanchard (R.) & Langeron (M.). **Nouvelles Recherches sur le Paludisme des Macaques d'après les Notes Posthumes de Xavier Bouniol.**—*Arch. de Parasit.* 1913. Mar. 12. Vol. 15. No. 4. pp. 599-607. With 1 coloured plate.

The authors state that Bouniol conducted a research on eight monkeys (*Macacus cynomolgus*) which were infected with *Plasmodium cynomolgi*. He unfortunately died at the end of a year's work before he had published his results.

The authors were, however, able to obtain most of his notes and give an account of his work, as gleaned from these. Of the eight monkeys employed by Bouniol four had their spleen removed. In two of these the splenectomy resulted in an acute exacerbation of the disease with increase of the plasmodia and death. In the other two the disease remained chronic, death taking place from an intercurrent disease after some months. The most interesting fact brought out in Bouniol's research is the effect of the splenectomy on the morphology of the parasite. Splenectomy resulted in the appearance of very amoeboid forms of the plasmodia, in which the protoplasm and chromatin were drawn out into long filaments. It also resulted in the production of an increased number of merozoites; as many as sixteen were produced instead of the usual eight. The other notable facts brought out by his research were, the constancy of the forty-eight hours' duration of the asexual cycle of the parasite, the constant appearance of Schuffner's granules in the infected red corpuscles, the variable pathogenic effect of this parasite on the infected monkeys, the rise of the temperature at the end of the infection, and the subnormal temperature shortly before death.

D. T.

BLACKWATER FEVER.

AFRICA. **Reports on Blackwater Fever in the Tropical African Dependencies.**—45 pp. With 2 maps. F'cap. 1912. London: Printed by H.M. Stationery Office.

The Secretary of State, on the suggestion of the Advisory Medical and Sanitary Committee for Tropical Africa, has circularised the Governors of the various East and West African colonies as regards the prevalence of blackwater fever in their respective territories. At present the conditions favouring the incidence of blackwater fever are not thoroughly understood and it has been considered that the collation and careful study of all cases which occur might throw some light upon the etiology of the disease and might suggest means for preventing or diminishing its occurrence. With this object the Secretary of State has requested that a special report may be forwarded annually by the Principal Medical Officer on all cases of blackwater fever occurring within the year in the colony, attention being particularly paid to the following points:—

"I. *Locality*:

"(*a*) Physical features (*e.g.*, swamps, bush, forest, &c.).

"(*b*) Occurrence of a series of cases in any one place, particularly in any one building, specifying dates and relation to native dwellings and intercourse.

"(*c*) Insect fauna; particularly biting or sucking insects such as mosquitoes and biting flies, ticks, bugs, lice, fleas, &c. Specimens should be obtained and identified where possible.

"II. *Seasonal Variation*:

(*a*) Marked or unusual climatic conditions.

"III. *Personal History*:

"(*a*) Medical history of patient (*e.g.*, previous diseases, attacks of malaria, habits regarding quinine-taking, &c.).

"(*b*) Previous movements of patient and personal conditions to which he has been subject.

"(*c*) Microscopic examination of the blood (noting relation of examination to stage of illness)."

Replies have been received from the Gambia, Sierra Leone, East Africa, Nyasaland, Uganda, the Gold Coast and Northern Nigeria. In addition to giving answers to the questions, some of the medical officers have written short accounts of their own personal views on the etiology of the condition and some have given clinical details of certain cases. Many of these are interesting and instructive.

An analysis of the answers given to the questions asked brings out very strongly the fact of previous attacks of malaria preceding the onset of blackwater fever. People who have suffered from many attacks of malarial fever and are also irregular in the taking of quinine are, without doubt, those who are attacked, but even regular quinine takers, if they have suffered much from malaria, may suffer, as the following cases show:—

An Asiatic suffered occasional attacks of malaria which, however were very mild. He took quinine very regularly. Blood examination in the attack showed a few malarial parasites of the tertian variety. These had disappeared from the blood by the

third day of the illness. His attack of blackwater fever was a mild one, recovery taking place about the tenth day.

In another case of blackwater fever, treated in hospital at Bathurst, the patient is said to have taken a regular dose of five grains of quinine per diem. He had been for three previous tours on the West Coast. In his first tour he contracted malaria and since that date suffered from slight attacks, those generally not lasting more than 22 hours. The attack of blackwater fever came on suddenly with violent vomiting and diarrhoea. The exciting cause seems to have been a dose of five grains of calomel taken that evening.

All Forde's blackwater fever cases, without exception, occurred in persons of some length of service in West Africa who had never taken quinine regularly as a prophylactic, but who, when they found malarial fever coming on, generally took two or three large doses of the drug and as soon as the fever had left them took no more until their next attack.

Manning says that there appears to be little doubt that those not using the daily ration of quinine are far more liable to the disease; in other words, haemoglobinuric fever is a manifestation of malarial toxicity.

Again, Hodges, speaking of Uganda, says that his reports appear to show a definite relation between blackwater fever and malarial infection, while in the medical case sheets of the other cases reported, the same thing is seen, viz.:—many attacks of malarial fever.

As regards the other points of information asked for in the circular, little can be deduced from the answers so far given, but the cases reported upon are comparatively few up to the present date. The insect fauna seems to be much the same wherever the cases occur and the same may be said of the physical features of the country in respect to swamps, bush, &c. The typical type of country for blackwater fever is apparently similar to that found where malaria prevails. The increasing frequency of the disease is due no doubt to the increase of susceptible individuals, *i.e.*, the increased white population which yearly goes to the endemic areas.

G. C. Low.

Stannus (H. Stannus). **The Etiology of Blackwater Fever.**—*Trans. Soc. Trop. Med. & Hyg.* 1913. Apr. Vol. 6. No. 5. p. 181.

The author states that during eight years in Nyasaland he has never seen blackwater fever in a native. His experience leads him to believe that in the absence of malaria there is no blackwater fever. He has seen no case of haemoglobinuric fever in which there had not been a previous attack of malaria treated by quinine. Several patients seen by the author have had three and four attacks of this disease.

D. Thomson.

Newell (A. G.). **The Etiology of Blackwater Fever.**—*Trans. Soc. Trop. Med. & Hyg.* 1913. Apr. Vol. 6. No. 5. pp. 177-181.

The author believes firmly in the relationship between blackwater fever and malignant tertian malaria. Quinine is not a cause of blackwater fever but may help to induce it at a time when the liver is extremely congested. In his opinion the haemoglobinuria is due to the intense congestion of the liver, caused by the malignant tertian parasites. If the condition of the liver is observed before giving quinine and if sufficient quinine is given regularly in intensely malarious districts there should be no blackwater fever. He agrees with Chalmers that there is a quinine haemoglobinuria and a malarial haemoglobinuria.

D. T.

Coles (Alfred C.). **Protozoal-like Structures in the Blood in a Case of Blackwater Fever.**—*Lancet.* 1913. May 3. pp. 1230-1232. With 1 text-figure.

The author made prolonged and repeated examinations of numerous films of blood, taken at all stages during a fatal attack of blackwater fever in a man age 28 who had just returned from Rhodesia. He was unable to find any malarial parasites or pigmented leucocytes, and no spirochaetes could be detected in fresh specimens under the dark ground illumination apparatus. In some of the blood films taken towards the latter stages of the disease a few peculiar granular bodies were found. The earliest period at which one of these bodies was seen was on the fourth day of fever, and then only a single example was found, but they were more frequent on the last day. These bodies were always exceedingly rare, about 4 were found in each film on the average; they were nearly always spherical, with a very definite outline. The protoplasm varied in tint from pale blue to bluish red. The diameter varied from 5μ to 17μ. They did not possess a nucleus, but contained within the protoplasm a number of small round or oval dots which stained a deep chromatin red colour. The number of dots found in each cell varied from 40 to 200. They measured $0{\cdot}3\mu$ to $0{\cdot}75\mu$ in diameter. Similar bodies were met with in the protoplasm of a few very large mononuclear leucocytes. The blood of the patient showed a large number of nucleated red cells and the haemoglobin amounted only to 14 per cent.

D. T.

Hand (Albert). **Malarial Hemoglobinuria — Report of Case.** — *Southern Med. Jl.* 1913. Mar. Vol. 6. No. 3. p. 171.

The author describes a case of malarial haemoglobinuria in a white girl aged 9 years. She had suffered from chronic malaria with anaemia and cachexia for two years and had had a previous haemoglobinuric attack five months before. After a malarial paroxysm two days previously the patient had a severe chill with immediate haemoglobinuria. This attack was severe and typical

with marked anaemia and severe vomiting. No parasites could be detected in the blood. The haemoglobin fell to 10 per cent., she became semi comatose, and developed a general oedema and paralysis of the right arm. Quinine was given in moderate doses, about six grains every twelve hours and under this treatment the urine cleared up. During the attack the blood showed a marked leucocytosis amounting to 80,000 white cells per cmm. The anaemia was very severe with 10 per cent. haemoglobin and 500,000 red cells per cmm. The transient paralysis was probably due to a localised oedema of the brain, a part of the general oedema. The patient appears to have recovered.

In the former haemoglobinuric attack quinine had been given six hours previously, but none had been given for fourteen days before the onset of the attack described.

D. T.

Stannus (Hugh Stannus). **The Treatment of Suppression in Blackwater Fever.**—*Jl. Trop. Med. & Hyg.* 1913. May 1. Vol. 16. No. 9. pp. 131-133. With 1 chart.

The author describes a case of blackwater fever in a European aged twenty-five in Nyasaland, in which there was complete suppression of urine.

He tried every measure possible to relieve this suppression without success and, as a last resort, operated on the left kidney, incising the capsule from pole to pole and the middle two-thirds of the organ itself. The result was that small amounts of urine (two and a half to four ozs.) were passed daily during the next four days. The patient however died. The author thinks it is probable that the patient might have recovered had the operation been performed earlier. All the cases of blackwater with complete suppression which he has known in Nyasaland have died without any sign of the suppression being relieved in the least degree. In such cases he wonders if it would be justifiable to operate early, since good results have been obtained by this procedure in cases of suppression in acute nephritis.

D. T.

da Matta (Alfredo Augusto). **A Febre Biliosa Hemoglobinurica no Amazonas e o seu Tratamento pela Cecropia.** [Bilious Haemoglobinuric fever in Amazonas, Brazil, and its Treatment with 'Cecropia.']—*Rev. Med. de S. Paulo.* 1912. Sept. 30. Vol. 15. No. 18. pp. 357-364. With 4 charts.

Blackwater fever is frequent in the Province of Amazonas. In all the cases haemoglobinuria was in evidence, though in varying degrees of intensity, the colour of the urine ranging from port wine colour to black. The author, whose cases numbered altogether 35, made the following observations:—

(1) Cases occurred after only a few months' residence in Amazonas. (2) There was a history of previous malaria in some form or other. (3) The absence of malarial parasites in certain phases of the disease was noted. (4) Pronounced anaemia leading to a leucopenia in the final stages of typical cases was evident.

The author explains the presence of haemoglobin in the urine, quoting Simpson and Ross. His observations are in accordance with those of Deaderick, who distinguished three phases, viz., (1) The attack is like one of malarial fever with parasites present in the blood and no haemoglobinuria. (2) Fever may be present, the parasites being generally absent, and haemoglobinuria appears. (During this phase the author made 24 blood examinations—all negative). (3) The post-haemoglobinuric stage with clear urine and fever, which if present is similar to that of a secondary attack of malaria, and generally no parasites are found in the peripheral blood. (The febrile attack during this phase was observed by the author in only three out of 35 cases.)

Quinine may be the cause of an attack of haemoglobinuria. The author found that in such cases haemoglobinuria sets in within three to six hours after its administration; beyond this time quinine is not responsible. The diazo-reaction and reactions of Gmelin and Grimbert are positive during the third stage.

The author found the best treatment to be the serum treatment of Gouzien. He also gives calomel, Vichy water, and lactate or chloride of calcium. The calcium salts, however, must not be continued for any length of time, as they will then give results contrary to those desired. 'Cecropia'* is considered invaluable. It eliminates bile and is a powerful diuretic. No bad effects were experienced even after a dose of 25 grams of the liquid extract.

Four charts are given.—Chart I is of a fatal case with *Plasmodium praecox* in the blood and intense albuminuria. It is not stated at which stage of the disease the parasites were present in this case. Charts II. and III. showed negative blood findings on the day before the onset of blackwater. Chart IV. is that of a case with *Pl. praecox* in the blood on the day before onset.

D. T.

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* *Cecropia palmata*, *C. peltata*, *C. baraensis* and other species are mentioned as occurring abundantly in Amazonas. It is not stated from which species the alkaloid (in the author's opinion a glucoside) is obtained.

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